A STUDY ON CORRELATION OF ADVERSE REACTIONS WITH CHANGES IN BIOCHEMICAL, HAEMATOLOGICAL AND PROCEDURAL PARAMETERS IN PLATELETPHERESIS DONORS

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LIST OF ABBREVIATIONS

AABB	American Association of Blood Banks
AC	Anticoagulant
ACD/ACD-A/	Acid Citrate Dextrose/Acid Citrate Dextrose - A/ Acid
ACD-B	Citrate Dextrose - B
ALL	Acute Lymphoblastic Leukemia
AML	Acute Myelogenous Leukemia
ATP	Adenosine Tri Phosphate
BCSH/	British Committee for Standards in Haematology/
BSH	British Society for Haematology
BMI	Body Mass Index
BP	Blood Pressure
Ca^{2+}/ tCa^{2+}	Calcium/Total Calcium
CABG	Coronary Artery Bypass Grafting
CBC	Complete Blood Count
CoE	Council of Europe
DGHS	Directorate General of Health Services
ECF	Extra Cellular Fluid
ECV	Extra Corporeal Volume
EDTA	Ethylene Diamine Tetra acetic Acid
ELISA	Enzyme Linked Immuno Sorbent Assay
FNHTR	Febrile Non Haemolytic Transfusion Reaction
Hb	Haemoglobin
Hct	Haematocrit
HLA	Human Leukocyte Antigen
HPCT	Haematopoietic progenitor cell transplantation
iCa/iCa^{2+}	Ionized Calcium
iMg/iMg^{2+}	Ionized Magnesium
IV	Intravenous
LDP	Leuco Depleted Platelet

MCS+	Mobile Collection System
Mg^{2+}/ tMg^{2+}	Magnesium/ Total Magnesium
MPV	Mean Platelet Volume
mRNA	messenger RNA
PC	Platelet Concentrate
PDW	Platelet Distribution Width
PLT	Platelet
PTH	Parathormone
RAAS	Renin Angiotensin Aldosterone System
RBC	Red Blood Cell
RDP	Random Donor Platelet
Rh	Rhesus
RNA	Ribo-nucleic acid
SDP	Single Donor Platelet
SPTR	Septic Platelet Transfusion Reaction
TBV/BV	Total Blood Volume/Blood Volume
TRAP	Trial to Reduce Alloimmunisation to Platelets
TTI	Transfusion Transmissible Infections
UK	United Kingdom
US FDA	United States Food and Drug Administration
VBD	Voluntary Blood Donation
VVR	VasoVagal Reaction
WB to AC ratio	Whole Blood to Anticoagulant ratio
WBC	White Blood Cell
WHO	World Health Organisation

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Introduction

INTRODUCTION

Apheresis is a procedure wherein whole blood removed from the body is passed through an apparatus that separates out one (or more) particular blood constituent and returns the remainder of the constituents to the individual's circulation.[1]

In Plateletpheresis procedure, a portion of donor's platelet and some plasma is removed with the return of donor's RBCs, WBCs and remaining plasma back into the circulation.[2] Plateletpheresis procedure allows collection of larger volume of platelets, thus increasing the ability to produce optimal component for the patient and prevents wastage.[1] It is estimated that 90% of the therapeutic platelet doses transfused in the United States of America are apheresis platelets. [3] One of the major indications for the usage of single donor platelets are in treating severe hypoproliferative thrombocytopenia due to haematological malignancies (AML, ALL), cytotoxic chemotherapy, hematopoietic cell transplant, congenital platelet function defects and in utilising HLA matched or human platelet antigen matched platelets to treat platelet refractoriness.[4-6]

The major advantages of using a single donor platelets are reduced multiple donor exposures leading to reduced risk of alloimmunisation, reduced incidence of transfusion transmitted diseases, higher quality product with a full and effective transfusion dose and a purer product in the form of Leuco-reduced platelets.[2] Usage of SDP product increases its purity in terms of decreased cellular contamination and also increases the overall yield of platelet collected.[7]

Although, apheresis procedures are considered to be safe procedures, the incidence of adverse effects in donors have not been determined at large. The adverse reactions encountered during plateletpheresis procedures include venipuncture related complications (hematoma formation), citrate toxicity (circumoral paresthesia, shivering, light headedness, twitching, tremors, nausea and vomiting, hypotension, carpopedal spasm, tetany, seizure) and vasovagal reactions with loss of consciousness.[8]

There have been limited studies regarding post donation haematological parameters, with one study reporting an increase in haemoglobin concentration, hematocrit and WBC count following a Plateletpheresis procedure whereas other authors described significant fall in these parameters. Although such reductions could be expected following plateletpheresis procedure, adverse clinical outcomes, such as thrombocytopenia and anaemia, as a result of these decreased counts should always be prevented.[9]

The biochemical changes that occurs following plateletpheresis procedures mainly include reduction in serum divalent cations, especially calcium and magnesium due to infusion of citrate anticoagulant resulting in hypocalcemic symptoms. The rapidity of plateletpheresis procedure is limited by the citrate toxicity. In order to enhance the operational efficiency and the level of donor comfort, calcium supplementation is required, either in the form of oral calcium supplements or intravenous calcium administration.[10,11] Also; the effects of intravenous citrate administration are more predictable and effectively counteracted with intravenous calcium infusions than with oral supplements.[12]

The amount of citrate reinfused into the donor depends on the following factors: centrifugation separation efficiency, amount and type of blood component returned containing citrate, the return speed, and the length of the entire procedure. Three procedural parameters influence the citrate concentration in the circuit: Inlet pump rate, AC flow rate and/or WB to AC ratio.[11]

A robust quality assurance system exists for donor safety by monitoring changes in blood count. Hence, this study is mainly aimed at attaining a safe donor profile by studying the effects of biochemical and haematological parameters in plateletpheresis donors and correlating the adverse events with changes in biochemical, haematological and procedural parameters.[13]

Aim & Objectives

AIM AND OBJECTIVES

Aim

To study the correlation of adverse reactions with changes in biochemical, haematological and procedural parameters in Plateletpheresis donors.

Objectives

- To study the changes in bio-chemical and haematological parameters in Plateletpheresis donors.
- To correlate the donor adverse reactions with changes in biochemical, haematological and procedural parameters.

Review of Literature

REVIEW OF LITERATURE

VOLUNTARY BLOOD DONATION & PLATELET UTILISATION

In a developing country like India, there is a constant demand for blood and its components owing to its large population, inspite of innumerable efforts taken by the Government, its agencies and non-governmental organisation in organising multiple voluntary blood donations. Under these circumstances, it is imperative to maintain a decent and a good number of voluntary apheresis donor bases to facilitate recruitment of platelet donors in times of insurgencies and emergency medical conditions. During such activities, it is important to maintain a good donor safety profile and to encourage an increase in repeat voluntary plateletpheresis donations.[14]

Platelets play a major role in maintenance of normal haemostatic activity and allogenic platelet transfusions are required for severely thrombocytopenic patients as supportive care. Collected platelets have a short shelf-life of only 5 days. The platelet discard rate on an average varies widely from around 20% - 67% in a hospital based setting. The possible reasons for such a wide discard rate are due to an expired unit, any undesired change in physical appearance, bag rupture, leakage during component preparation, loss of swirling, mishandling during storage or a reactive sample. Hence, there is an inadvertent difficulty in recruiting more number of voluntary non remunerated whole blood donors to compensate for the shortcomings in the demand – supply chain of providing platelets to the concerned specialties.[15]

In hospitals with low platelet demand, platelets may be prepared on demand basis which can be obtained from apheresis (SDP) platelets providing better quality and quantity as compared to random donor platelets (RDP). Otherwise, separation of whole blood into packed cells and plasma should suffice. This also ensures saving on the extra cost of triple blood bags used for this purpose, as against usage of single blood bag for 'Whole Blood' and double blood bag for packed cells and plasma and their associated costs.[16]

The nation's focus on Voluntary Blood Donation was primarily on whole blood donation until now, but little attention has been focussed on apheresis donors recruited to the blood bank by patient's attendants. Apheresis platelets are being currently prepared from patient's relatives and/or friends. Experts have opined that blood bank services needs to be expanded in covering apheresis donors and rare blood group donors and momentum in voluntary plateletpheresis donations needs to be initiated at the earliest.[14]

To alleviate and compensate for the demand supply chain, there is a slow transition from whole blood donation towards apheresis donations as seen in many developed countries, especially platelet donations, considering the short shelf life of platelets (5 days) and difficulty in recruiting voluntary non remunerated blood donors.

EPIDEMIOLOGY OF VBD – THE GLOBAL & INDIAN SCENARIO:

A total of 112.5 million blood donations are collected globally with 50% being collected in high income countries (19% of world population). The median annual donations per blood centre vary from 16,000 in high income countries as

against 5400 in low- and middle income countries. Fewer than 10 donations per 1000 people have been collected from 70 countries, in which 6 low – or middle income countries fall under South- East Asian region. The blood donation rate in high-income countries is 33.1 donations per 1000 people; 11.7 donations in middle-income countries and 4.6 donations in low-income countries.[17]

In the era of component therapy, still many low- & middle- income countries have been found utilising only whole blood therapy significantly. This is evident from the data that the capacity to provide patients with different blood components ranges from 43% collected in low income countries, 78% in middle income countries to 96% in high income countries.[17]

In South East Asia region, only around 15.9 million units are collected every year as against an annual estimated requirement of 18 million units per year. Blood donation through voluntary blood donors contributes around 82% and 100% of collected blood units are screened for transfusion transmitted infections.[18]

India, being the second most populous country across the world with a population of 1.2 billion, the country still faces a blood shortage of 3 million units. The joint efforts of the government, non-governmental organisations and staff in the blood transfusion services have seen a slow ascending transition in the status of voluntary blood donation (VBD) in our country. In the year 2006-07, VBD was only 54.4%, it increased steadily to 59.1% in 2007-08, 61.7% in 2008-09, 74.1% in 2009-10 to 79.4% in 2010-11 and 83.1% in 2011-12.[19]

The issue of blood shortage is due to lack of voluntary blood donors and figures have been found rising in states like West Bengal, Maharashtra, Tamil Nadu, Gujarat, Chandigarh and Himachal Pradesh. Health experts are of the opinion that these shortages can be overcome, if an additional 2% (two percent) of Indians donated blood.[19]

PLATELETPHERESIS IN WORLD

Since the introduction of automated apheresis in the Unites States, transfusion of single donor platelets exceeded collection of whole blood derived platelet concentrates in the year 1994. Data in 1997 shows increase in utilisation of single donor platelets by 31.7%.[20]

In developed countries like the United States of America, there has been an increase in apheresis platelet collection by 18.1% as against a decline in whole blood derived platelets of 10.3%. In 2011, 91.1% of platelet doses collected was by apheresis technique. This shift is attributed to optimise the products collected based on the donor's characteristics and inventory needs.[8]

RDP VS SDP

Even though, platelet concentrates (PC) derived from whole blood collections was the initial standard of care, the medical necessity for development of apheresis procedure was driven by the fact that many patients become alloimmunised on frequent platelet transfusions and require platelets from donors with specific human leukocyte antigen (HLA) types. There is a controversial debate being currently pursued regarding the type of platelet product to be used (i.e.)

whether to go for RDP or SDP. Single donor platelet utilisation is immense as seen by a 6.4% increase in SDP usage from 1997 to 1999 in the US and is of particular value while treating advanced conditions like hematopoietic progenitor cell transplantation, coronary artery bypass graft patients, solid organ transplants and trauma.[21,22]

The most common adverse reactions noted among utilisation of platelet concentrates for transfusion includes occurrence of Septic Platelet Transfusion Reactions (SPTR), febrile non haemolytic transfusion reactions (FNHTR), allergic transfusion reactions, platelet alloimmunisation and platelet refractoriness.[21]

Studies have found that SDP has a slight edge over RDP in the form of easy in-line process leukoreduction reducing incidence of FNHTR, decreased risk of Septic Platelet Transfusion Reaction (SPTR), treatment of alloimmunised patients preventing platelet refractoriness, increasing the transfusion interval between two dosages and finally SDP is the treatment of choice for Hemato-oncology patients requiring frequent platelet transfusions. The rate of occurrence of SPTR is 5 times higher among PC pool recipients as compared to SDP recipients. Usage of SDP over RDP has shown a threefold reduction in occurrence of SPTR. The same study also found that SDP accounted for 17% of all platelet transfusions with a reaction rate of 1.78% as compared to 4.51% reaction rate noted with PC.[21]

SDP transfusions have the advantage of reduced donor frequency exposure, reduced risk of infectious disease transmission and transfusion reactions as compared to pooled RDP transfusions provided to the patients. Process leukodepletion helps to decrease the amount of cytokines which is responsible for

causing FNHTR released during storage. Trial to Reduce Alloimmunisation to Platelets (TRAP) study results suggests leukodepletion to be a practical method to reduce alloimmunisation. It was observed that there was no significant advantage of SDP over PC for the prevention of alloimmunisation.[21]

The major limitation regarding the utilisation of SDP over RDP is the 'cost factor' which plays a major role in developing country like India. Also, the increased demands of SDPs have stressed on the need for eligible platelet donors from whom quality product of optimum yield can be harvested to achieve maximum increments in a recipient.[7, 22]

APHERESIS – DEFINITION & TYPES

Apheresis is derived from a Greek word "Aphairos" which means "to separate" or "to remove" and was first used in the year 1914 by Able, Rowntree and Turner. Apheresis is broadly classified into two major types viz., 'Cytapheresis' meaning removal of cellular elements and 'Plasmapheresis' meaning removal of plasma and its products.[8]

Plateletpheresis procedures (SDP) produce an average equivalent of 6-10 units (3-5 x 10^{11} platelets) of random donor platelet concentrates at one time and have become the main source of platelets in many countries.[22]

PLATELETPHERESIS DEVICES

An ideal apheresis machine is considered to be one that permits simple set/kit placing, allows donations to be performed quickly with few adverse effects, requires little attention from operators (highly automatic) and in which the final

products are homogenous and comply with the requirements laid down by blood bank regulations. Improvements in apheresis systems are directed at obtaining faster apheresis processes with fewer adverse events for donors, and production of high quality products.[23]

The earliest centrifugation device used for commercial purposes was the "hand cranked cream separator" invented in Sweden in 1877 by Dr.Carl Gustav Patrik De Laval. The first basis for a cell separator arose from Dr.Edwin J. Cohn's works on making of biomechanical equipment for immediate separation of blood components named as the "Cohn centrifuge". Subsequent technical modifications to the centrifuge led to development of a bowl named "Latham Bowl" named after Allen Latham Jr. This was followed by development of another blood cell separator – "NCI-IBM Blood Cell separator" under the directorship of Dr.Emil.J.Freireich. Later, a sealless continuous flow centrifuge was developed by Dr.Yoichiro Ito which prevented platelet deterioration in long term plasmapheresis. The other earlier apheresis devices developed were the Aminco celltrifuge II, Fenwal CS 3000, IBM 2997/COBE Spectra, Membrane plasma separation cell separators.[25]

EARLIER APHERESIS DEVICES

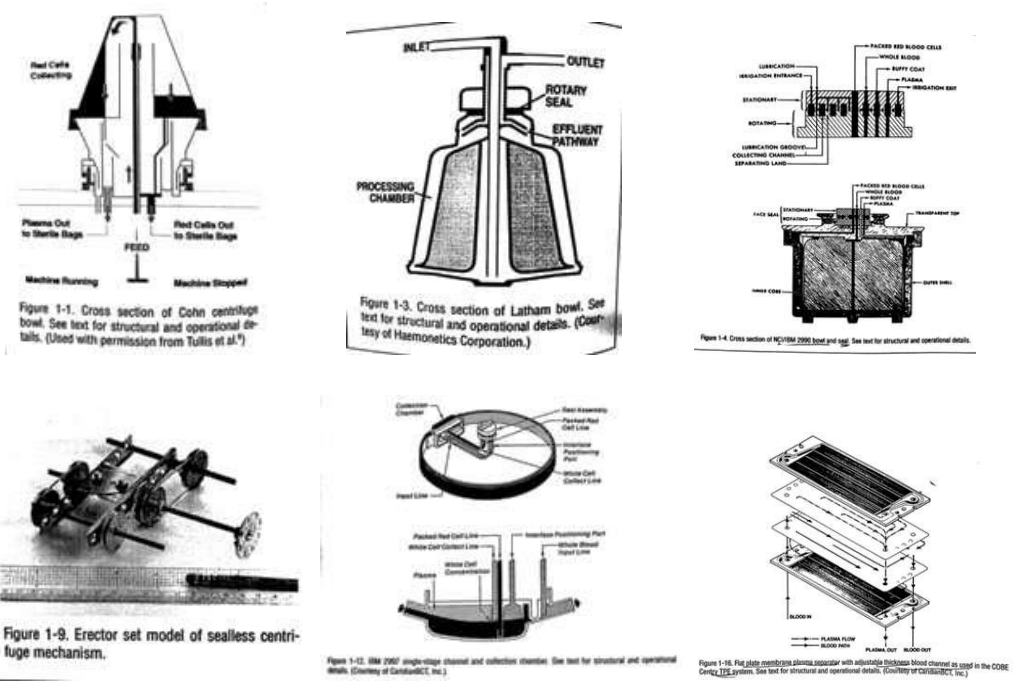

Fig. 1: List of Early Apheresis devices[25]

Plateletpheresis devices functions on the principles of centrifugation – either intermittent flow centrifugation or continuous flow centrifugation. Intermittent flow centrifugation works in cycles, with blood taken from the donor, spinning/processing it in the machine and returning the unwanted/ remainder of the blood components back into the donor. In intermittent flow devices (also called discontinuous or semi continuous flow), blood is processed in discrete batches. Separation can occur until the separation container is filled with the most dense component; then the container must be emptied before the next batch is processed.[13, 26]

Continuous flow centrifugation usually requires two venipunctures since the word "continuous" indicates that collected, spun/processed and returned blood are occurring simultaneously. In continuous flow devices, low-, high-, and intermediate-

density fractions can all be removed in an ongoing manner so that the separation container need not be emptied until the end of the procedure. Newer generation continuous flow centrifugation based apheresis machines are using only single venipuncture based access.[13, 26]

Continuous flow cell processing instrument for plateletpheresis provides a continuous and more controlled rate of citrate infusion. The major advantage of continuous flow cell separator is the low extracorporeal volume being used in the procedure and reduced donor turn-overtime favouring more compliance from the donors for repeat donations.[13, 24]

The basic steps in apheresis are (i) separation of blood components & (ii) removal of desired component(s) using an online automated system. Based on the principle of centrifugation and the specific gravity of various blood components, the mature red cells (most dense component) would be located at the bottom and plasma (least dense component) would have risen to the top. In between, in order of decreasing density, would be neocytes (young red cells), granulocytes, mononuclear cells and platelets. The granulocyte fraction contains neutrophils, basophils and eosinophils. The mononuclear cell fraction contains lymphocytes; monocytes, peripheral blood progenitor cells, and in some leukemic patients, blast cells.[26]

The newer generation of blood cell separators are equipped with leucofilters thus enabling effective leukoreduction of platelet concentrates. The high degree of separation between donor platelets and leukocytes are because of various principles employed, namely – flow path geometry, counter flow centrifugation, elutriation and separation of fluid particle bed based on the difference in cell mass.[13]

Technical advancement in automated cell separators has improved the productivity and quality of the apheresis platelets collected. Newer devices showed small range of collection variability and more consistent platelet production as compared to the older devices that resulted in lower platelet deficit.[27]

The transfusion medicine specialist is concerned with the collection of platelets as well as optimising the product in terms of balancing the platelet yield with pre-donation and post-donation haematological changes in the donors.[28]

There are various cell separators available currently each with its own advantages and disadvantages. The major advantage of Haemonetics MCS+ cell separator is the user friendly approach in installing the kits, reduced cost per kit as compared to other cell separator kits, portability factor and single arm venous approach which makes the procedure comfortable for the apheresis donors. In a study on 40 plateletpheresis donors comparing the preparation of platelets and its donor adverse reactions between two cell separators, Haemonetics MCS+ was recommended to be a better choice as compared to Baxter CS 3000+ cell separator.[22]

The duration of the procedure has been identified as the most important element in the apheresis platelet donor retention and is one of the important factors in evaluating the apheresis system. In a study on 51 plateletpheresis donors evaluating the best apheresis systems among Haemonetics MCS+, Trima Accel and Amicus, it was concluded that most of the donors preferred Trima Accel due to its relatively shorter duration of the procedure. Also, Amicus was shown to be the most efficient in terms of platelet separation.[23]

PHYSIOLOGY OF PLATELETPHERESIS PROCEDURE

Physiology of platelets

Platelets are non-nucleated cells derived from highly controlled disintegration of the cytoplasm of megakaryocytes. Megakaryocytes are the giant platelet precursor cells in the bone marrow. Platelets play a pivotal role in maintaining haemostasis through its two major functions – (i) adhesion to exposed sub-endothelium with subsequent formation of aggregates at site of vessel injury, and (ii) facilitation of thrombin and fibrin formation to strengthen the aggregates. In normal individuals, approximately 82% of platelets complete their entire life cycle of 10.5 days leaving the circulation by a process called senescence which is incompletely understood. The remaining 18% leave the circulation prematurely in response to ongoing haemostatic needs such as spontaneous haemorrhage. The fixed daily loss of platelets is approximately 7100 platelets /µL. Generally, the survival time of platelets is shorter at lower platelet concentration presumably because of increasing fraction of circulating platelets being consumed per unit time to meet ongoing haemostatic needs.[4]

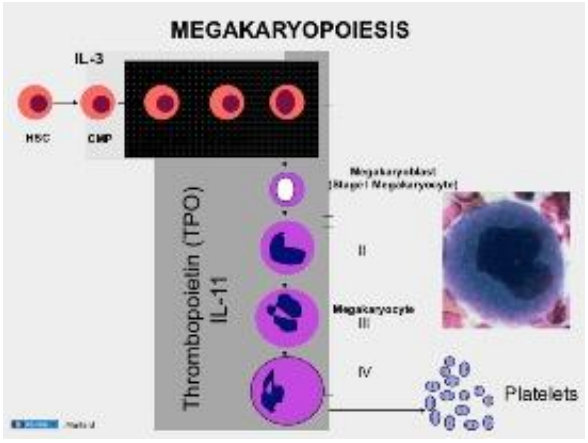

Fig.2: Megakaryopoiesis and platelet production

There exists a tight regulation of total platelet mass with a relationship between peripheral platelet concentration and total body platelet mass. Mean volume for individual platelets is inversely proportional to the platelet concentration. Two-thirds of the entire platelet body mass is present in the circulation and the remaining one-third sequestered in the splenic pool. Exchangeable equilibrium exists between the splenic pool and the peripheral blood platelets. Splenic platelet sequestration is proportional to the organ blood flow and is affected by donor hematocrit, adrenergic state and as yet undefined factors. Finally, it is the blood concentration that dictates the number of platelets available to the apheresis instrument, which is further dependant on individual variability in the immediate release of platelets from the splenic pool.[4]

- ***Role of anticoagulant***

  - **Normal Calcium homeostasis**

99% of total body calcium is present in bone as hydroxyapatite crystals. A small proportion of skeletal calcium is in non crystalline form which can be rapidly mobilised for an extraosseous deficiency. All of the 1000 mg of non osseous calcium is extracellular with normal plasma concentration being 10 mg/dl (2.5 mmol/L). 40% of plasma calcium is bound primarily to albumin; 13% complexes with citrate, phosphate & lactate and the remaining 47% of plasma calcium are unbound called as ionised calcium or free calcium. (1.2 – 1.3 mmol/L).[29]

The percentage (%) of anion bound calcium is markedly increased when exogenous anions are introduced (citrate). Since ionised calcium participates in coagulation reactions, citrate infusion results in decreased ionised calcium which is

responsible for the anti-clotting effect and adverse symptoms associated with citrate anticoagulants.[29]

Fall in ionised calcium leads to increase in parathormone secretion stimulating calcium mobilisation from bones, non crystalline pool and resorption from crystalline pool. Further, parathormone increases absorption of calcium from intestine and renal tubules.[29]

❖ **Physiological effect of citrate infusion in plateletpheresis**

Anticoagulation plays a primary role for maintaining the fluidity of extra vascular/extracorporeal blood and patency of the apheresis circuit. Citrate containing ACD solution is the preferred anticoagulant of choice due to its low cost, safety, and rapid systemic clearance as compared to another anticoagulant, heparin. The anticoagulant effect of citrate results in reversible chelation of divalent cations - Ca^{2+} and Mg^{2+} and their sequestration from their normal physiological function.[11]

Exogenous citrate is rapidly metabolised by Kreb's tricarboxylic acid cycle in the mitochondria of the kidney, liver and skeletal muscle. During plateletpheresis procedure, in the extracorporeal circuit, citrate concentration of 15-24 mmol/L reduce ionised calcium levels sufficiently to 0.2 – 0.3 mmol/L to impair haemostasis and produce an anticoagulant effect.[11]

Metabolism of one citrate molecule results in release of bound calcium, consumption of three hydrogen ions and release of three molecules of bicarbonate, which contribute to blood alkalinity. About 18-20% of infused citrate remains

unmetabolised and excreted by kidneys. In the presence of normal hepatic metabolism, the half – life of infused citrate is 36±18 minutes.[11]

Various citrate formulations are used during apheresis procedures, out of which, commonly used formulations are ACD – A (Acid Citrate Dextrose – A) and ACD – B (Acid Citrate Dextrose – B), both of which contains citric acid, sodium citrate and dextrose. ACD-A contains 3% citrate (112 mmol/L or 21.3 mg/ml of citrate) and ACD-B contains 2% citrate (68 mmol/L or 12.8 mg/ml of citrate). There are two aspects of citrate infusion during plateletpheresis – rate of anticoagulant delivery to the donor mediating systemic effects of citrate and rate of anticoagulant delivery in the circuit for maintenance of effective anticoagulation in the extracorporeal circuit.[11]

Donors can tolerate upto 20% decline in ionised calcium levels permitting higher citrate infusion rates and shorter runs. Most of the current instruments control AC infusion rates which are based on Total Blood Volume (TBV) and they maintain citrate delivery rates between 1.0 to 1.8 mg/kg/min. Three procedural parameters influence the citrate concentration in the circuit: Inlet pump rate, AC flow rate and/or WB to AC ratio. Higher AC ratio favours development of platelet clumping and interface stability and lower AC ratio (<10) results in greater concentration of anticoagulant delivered to the patient increasing symptoms of citrate toxicity. The amount of citrate reinfused into the donor depends on the following factors: centrifugation separation efficiency, amount and type of blood component returned containing citrate, the return speed, and the length of the entire procedure.[11]

Although citrate anticoagulation is considered safe with uncommon serious side effects, chelation of cations continues in systemic circulation resulting in metabolic complications like hypocalcemia, hypomagnesemia, metabolic alkalosis and electrolyte derangements. Mild citrate related reactions such as perioral tingling or paresthesias have been reported to be the most frequent complication. Citrate related complications have been reported to occur in 1.2% of donors during voluntary donation, 7.8% of patients undergoing therapeutic plasma exchange procedures and 48% of patients undergoing large volume leukapheresis during peripheral blood progenitor cell collection.[11]

❖ **Calcium homeostasis during plateletpheresis**

Citrate ions have moderate affinity for binding calcium at physiologic pH. The important factors that prevent profound hypocalcemia are dilution, redistribution, metabolism and excretion of the infused citrate. During a plateletpheresis procedure, there is 23-33% reduction in ionised calcium when citrate levels are in the range of 17 mg/dl to over 30 mg/dl. This might be due to an obligate increase in excretion of the cations (calcium, magnesium, sodium, potassium) following renal excretion of acute citrate load. Serum citrate levels returns to baseline within 4 hours after cessation of infusion.[29]

There is a rapid rise in parathormone levels within 5-15 minutes of citrate infusion and then it levels off or slightly decreases during the rest of the procedure. PTH raises calcium levels by – (a) releasing calcium from large reservoir contained in the bones, (b) enhancing the active reabsorption of calcium in the kidney and (c) enhancing calcium absorption in small intestine by increasing the production of

activated vitamin D. The net effect of endogenous parathormone and exogenous citrate leads to rapid decrease in total calcium during the first 15 minutes of the procedure attaining a 25% decrease by 90 minutes following a safe citrate infusion rate of 65-95 mg/kg/hr. In addition to body weight, hematocrit and blood volume, citrate toxicity may also be affected by duration of infusion. Based on this, an expert panel recommended citrate infusion to be limited to 90 to 110 minutes for platelet collections.[29, 31]

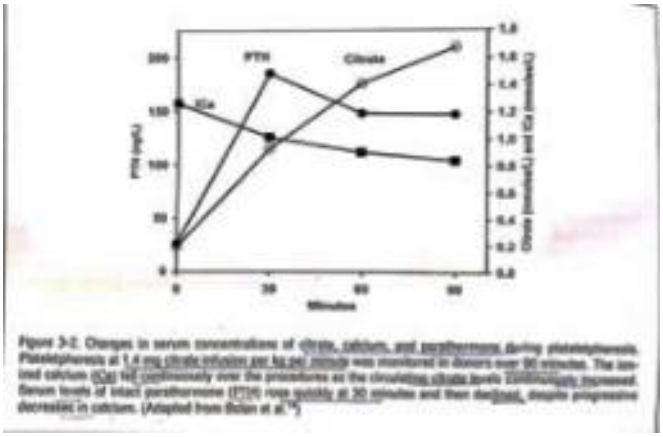

Fig. 3: Changes in serum concentrations of citrate, Ca^{2+} and PTH during plateletpheresis[29]

Calcium supplements are frequently administered to plateletpheresis donors to counteract acute citrate related symptoms and decreases in ionised calcium levels. Calcium ingestion significantly reduces the extent of decline in iCa and iMg levels but the effects are dose limited, transient and modest in magnitude compared with the changes induced by infusion of intravenous citrate solution. Also, other factors like donor specific variations in initial divalent cation reserves, capacity for divalent cation mobilisation and pace of citrate metabolism during apheresis procedure offered more protective effects against citrate mediated decrease in iCa and iMg

levels. Also, calcium and magnesium bound to albumin at the beginning of apheresis procedure acts as a reservoir to counteract acute citrate mediated decrease in ionised levels of cations.[12]

The protective effect against citrate toxicity includes a more rapid metabolism and redistribution of citrate during apheresis, higher baseline divalent cation levels (including albumin bound reserves) and a greater capacity for intra-apheresis divalent cation mobilisation.[12]

In a study conducted on 23 donors who underwent four plateletpheresis procedures each, it was observed that usage of 2 g calcium carbonate dose as compared to placebo produced a significant increase in intra apheresis divalent cation levels and a trend towards reduced donor symptoms. Also, an intravenous calcium infusion effectively counteracts the effects of intravenous citrate administration as compared to the oral supplements. Since most of the plateletpheresis procedures were associated with only minimal or no donor symptoms, routine administration of oral calcium before plateletpheresis is not recommended. However, administration of 2 g oral calcium carbonate tablets , 30 minutes before the apheresis procedure may be recommended for donors with prior history of clinically significant citrate related effects or for high risk groups (female donors receiving high citrate infusion rates).[12]

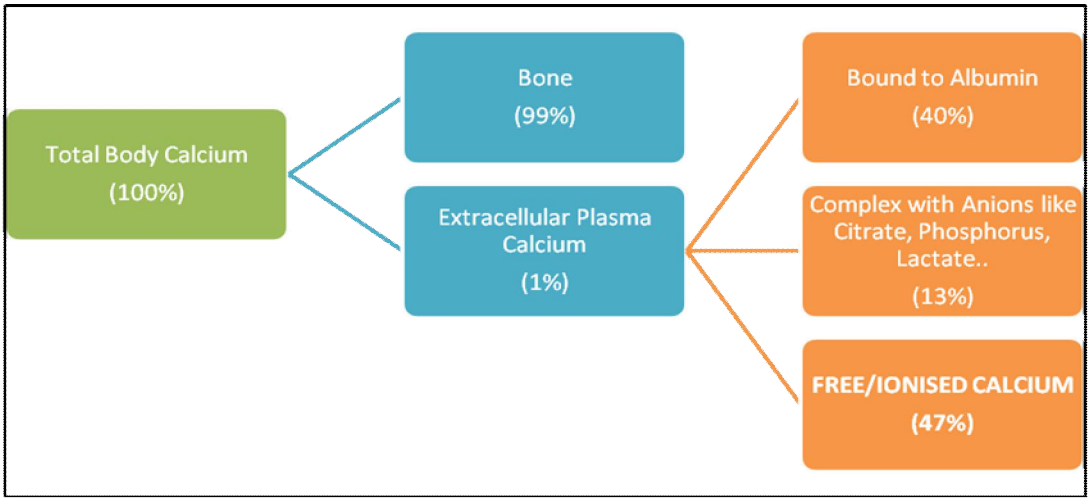

Fig 4: Overview of Calcium Distribution in Human Body

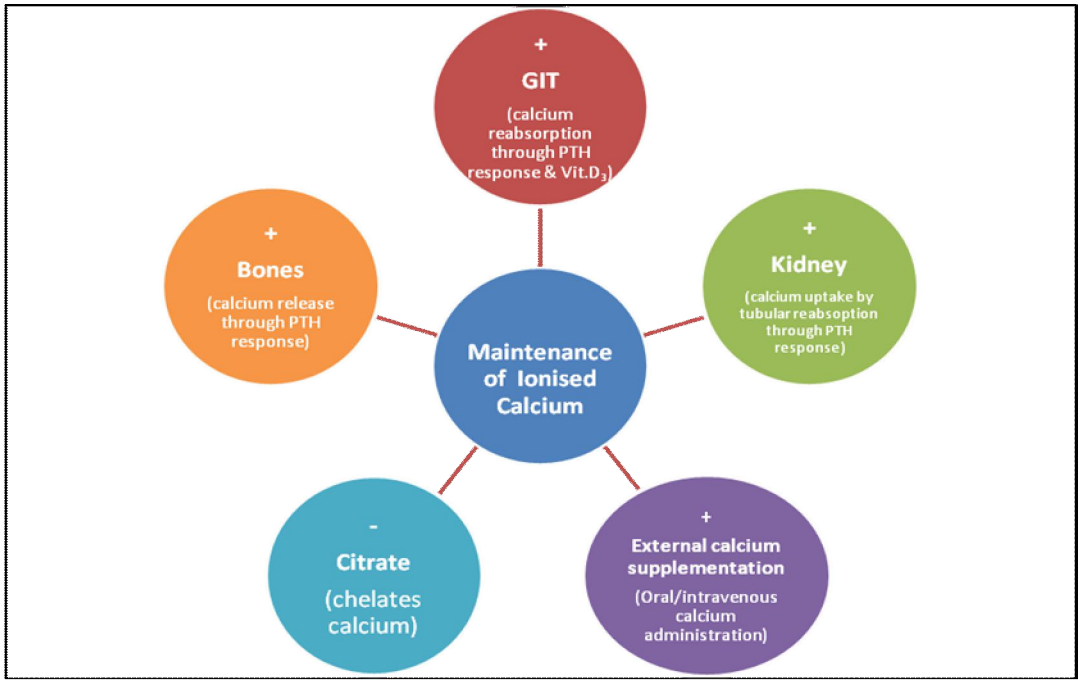

Fig. 5: Calcium Homeostasis during Plateletpheresis procedure

❖ Magnesium deficiency and plateletpheresis

Approximately, 55% of total magnesium lies within the skeleton and 45% is intracellular. Within the cell, it is one of the most prevalent cation. The concentration of intracellular magnesium is approximately 2.4 to 7.3 mg/dl or 1 to

3 mmol/L. The intracellular magnesium is bound to proteins and negatively charged molecules, especially ATP. Extracellular magnesium accounts for 1% of total body magnesium content and about 55% of free plasma magnesium exists.[32]

Citrate chelates magnesium and calcium. Infusion of citrate resulting in hypomagnesemia is usually seen in large – volume progenitor cell collections with mean ionised magnesium levels falling by 39% below baseline in the non supplemented group and decline of 7.4% in intravenous magnesium supplemented group. However, prophylactic magnesium supplementation is not recommended for plateletpheresis donations.[29]

During repeated platelet donations or during prolonged plateletpheresis procedures, accumulation of citrate outpaces its metabolism leading to hypocalcemia or hypomagnesemia causing significant donor discomfort which may require hospitalisation at times.[33]

- ***Role of fluid shift***

  - **Hemodynamic changes during plateletpheresis procedures**

Fluid shifts can occur either during whole blood removal or when one or more components are retained and the remainder being reinfused back into the circulation with or without replacement solutions. These changes in intravascular volume can induce hemodynamic alterations. Especially in therapeutic procedures, dilutional effects on plasma constituents are seen. Hemodynamic changes are markedly observed during therapeutic plasma exchange due to utilisation of replacement fluids like albumin as compared to plateletpheresis procedures. However, minor fluid shifts can occur as a physiological response to

plateletpheresis. A relatively small net volume deficit of approximately 300 ml plasma develops gradually over 60-100 minutes during a simple plateletpheresis procedure.[29]

- ***Role of cellular loss***

❖ **RBC count and Plateletpheresis**

First generation or earlier generation of apheresis devices causes larger amounts of red cell loss during plateletpheresis procedure as compared to the recent generations of apheresis devices. The loss of red cells was attributed to the following factors, namely, viz. – (a) blood loss in the void volume of apheresis kit at the end of the procedure; (b) mechanical haemolysis by pressure pumps; (c) anaemia caused by haemo-dilution due to infusion of saline and citrate solutions during the apheresis procedure.[9,34]

It was also opined that hyperlipidemia or unclear blood stream could be possible reasons for platelet products being contaminated with red cells.[22]

❖ **WBC count and Plateletpheresis**

During utilisation of earlier apheresis devices, there was a potential depletion of lymphocytes and platelets leading to immunosuppression and haemorrhage among volunteer donors. This resulted in publication of donor selection criteria and guidelines for minimum donation intervals. The extent of lymphocyte depletion has been markedly reduced with subsequent technical modifications to automated apheresis instruments.[20]

❖ Platelet count and Plateletpheresis

Most of the studies have concluded that although sustained reduction in platelet count is expected to be seen after plateletpheresis procedure, donors presenting with clinical thrombocytopenia is unlikely.[13]

It was observed that there is an expected significant and sustained decrease in platelet count of about 50,000/ µL after plateletpheresis procedure and correlates directly with frequent plateletpheresis donors. There was a 10 – 20% decrease in platelets in these kinds of frequent donors with a small proportion developing clinically significant thrombocytopenia. When older apheresis devices were used, there was a 20%-30% decrease in platelets being noted and were transient in nature. Baseline platelet counts were higher in female donors.[20]

During a plateletpheresis procedure, a higher initial platelet count of the donor and a shorter duration of the procedure results in higher yield of platelets collected.[38] In a study conducted on 50 first time plateletpheresis donors in South India, it was observed that post donation platelet count dropped significantly in all the 3 groups (pre-donation platelet count: Group I- 1.5 L/µL to 2.2 L/µL; Group II- 2.2 L/µL to 2.75 L/µL; Group III– 2.75 L/µL to 3.5 L/µL) with a stimulus from spleen for recruitment of platelets existing only in the 1st group. This was attributed to the platelet count being depleted more in the 1st group as compared to the 2nd or the 3rd group leading to a strong recruitment signal from the spleen to recruit platelets from the storage pool. It was also concluded that the donor's platelet count returned back to baseline by Day 7 and a slight increase above baseline by Day 14 in majority of the donors.[35]

Recent trends to reduce the cost associated with plateletpheresis collections and to reduce the donor exposure frequencies have been to collect “double” and “triple” collections from individual donors. However, such collections over a long term period are likely to diminish the recruitment of voluntary plateletpheresis donors. This highlights the critical importance of regular and close monitoring of pre-apheresis platelet counts in serial donors along with tightly regulated donor deferral policies.[20]

Although FDA guidance regulations restrict the number of platelet donations during double & triple product collections, a study conducted on 953 donors in a regional transfusion centre states that it may not appear necessary to impose somewhat complex inter-donation intervals according to number of components produced at prior donations and that it would have an adverse impact on the supply of apheresis platelets. It was stated that the haematological changes that occur also depends on the materials used in apheresis kits and the instrumentation used during plateletpheresis procedures.[36]

Female donors tend to have higher baseline platelet count as compared to their male counterparts, but due to their lower blood flow rates that contribute to longer processing time and a high collection rate per kilogram body weight, it was observed that platelet losses were higher in female donors as compared to male donors. Differences exist in the collection efficiency between short term and long term procedure and were attributed to the reduced collection efficiency at the beginning of apheresis procedure, until the blood to plasma interface is well positioned. This aspect was not yet considered in plateletpheresis software concerning calculation of the target.[27]

It was also observed that gender also influences platelet yield and female donors tend to have higher platelet yield. The reason attributed to it may be due to higher prevalence of iron deficiency among female donors and role of hormonal influence on the platelet count.[37]

Platelet recruitment is a compensatory response for the platelet loss that occurs during plateletpheresis procedure. Upon removal of platelets from the peripheral blood, the circulatory blood pool is effectively replenished from the splenic platelet pool which constitutes about one-third of the entire platelet population and is in exchangeable equilibrium with the peripheral circulatory blood component. This finding was supported by studies on differences in platelet recovery between normal blood donors and splenectomised patients supporting the findings that apheresis platelets are redistributed from spleen.[27]

Rogers and co-workers observed that donors with low – normal platelet counts can safely donate satisfactory platelet units by extending the collection time. Safety of frequent apheresis donors and prevention of thrombocytopenia with possible haematological complications can be prevented by maintaining strict institutional deferral policies. It was also observed that although thrombopoietic response occurs days after plateletpheresis, short term effects in course of apheresis could affect final platelet yields.[27]

- **Hematocrit and Plateletpheresis**

In a study conducted on 258 plateletpheresis procedures, it was observed that haematocrit value of the donor had no effect on the duration of separation but had an impact on the efficiency of platelets collected. Increased haematocrit values

significantly reduce the efficiency of platelets collected. During plateletpheresis procedures, donors recruited with higher baseline platelet count with lower haematocrit values results in a better product collected with higher yield, having lower duration of separation and increasing the efficiency of platelet collection.[38]

Pre-donation Haemoglobin is another significant factor that influences platelet yield and most of the studies have observed a statistically negative correlation with platelet yield and the reason was probably due to higher plasma volume processed in donors with low haemoglobin concentration leading to higher platelet yield.[7, 28]

In a study conducted on 457 healthy first time plateletpheresis donors on five different apheresis systems, a drop in haemoglobin and hematocrit was attributed to the haemodilution due to infusions of citrate anticoagulant solutions and saline.[9]

A correlation between haemoglobin concentration and platelet yield provides mixed response among various studies with certain studies quoting that there exists an inverse relationship between haemoglobin concentration and platelet count and other studies quoting no correlation existing between them. The reason attributed to their inverse relationship may be due to higher plasma volume being processed in donors with low haemoglobin concentration and thus providing a higher yield.[37]

In a study conducted on 171 plateletpheresis procedures, a significant 1.7% increase in post donation haemoglobin was observed and was attributed to concentrated red cells being returned to the donor and 200-300 ml of plasma retained at the end of the procedure. Another explanation offered for such increase

in post donation haemoglobin values are the time of collection of second sample (i.e.) the time lag between the end of the procedure and obtaining sample allowing the impact of compensatory physiological mechanisms to come into action and the type of cell separator used.[28]

❖ **MPV, PDW and Plateletpheresis**

A study on 271 plateletpheresis procedures indicates a direct negative correlation between donor pre-donation MPV and yield of SDP. The possible reasons was attributed to the separation mechanism of the automated cell separators (i.e.) as the platelet size increases, these larger platelets are excluded from collection mimicking as red cells and so smaller platelets are collected more efficiently by automated cell separators yielding a better product.[28,39]

Studies have observed either, a no significant change or a mild decrease which was not significant in the post donation values of platelet distribution width at the end of the procedure.[28]

DONOR SELECTION CRITERIA

Recruiting donors based on eligibility criteria as per various recommendations is to ensure and protect voluntary blood donors from too aggressive blood donation practices and to protect the recipients from transfusing blood products below the minimal quality requirements.[34]

According to Drug & Cosmetics Act,1940 & Rules 1945, donors shall be selected based on the same criteria as that of whole blood donation and in addition shall follow the following criteria, namely, viz.,

(a) At least 48 hours must elapse between successive apheresis and not more than twice in a week. [40]

(b) Extracorporeal blood volume shall not exceed 15% of donor's estimated blood volume. [40]

(c) Plateletpheresis shall not be carried out on donors who have taken medication containing Aspirin within 3 days prior to donation. [40]

(d) If during plateletpheresis or leukapheresis, RBCs cannot be re-transfused then at least 12 weeks shall elapse before a second cytapheresis procedure is conducted.[40]

According to Swiss regulation, donor's pre-donation haemoglobin concentration is the only lab parameter considered for selection of blood donors. European and American guidelines allow donating whole blood if haemoglobin concentration >12.5 g/dl.[34]

The 1990 UK guidelines for assessing suitability of voluntary apheresis donors in repeating the apheresis procedures recommend regular analysis of complete blood count, total protein and albumin in repeat apheresis donors. The Drug and Cosmetics Act in India do not have such established guidelines.[9]

A minimum interval of 48 hours is required between successive plateletpheresis donations, not more than twice a week and not more than 24 times a year. A pre-platelet count for single and double apheresis platelet collections is not required according to AABB standards. If the frequency of donation is within 4 weeks of last donation, a pre- donation count is required. Most of the guidelines

regarding frequency of plateletpheresis donations are derived from the West. Hence, it is time to evolve and make tailor-made guidelines applicable and suitable to our Indian population.[35, 41]

According to FDA draft guidance titled "Collection of Platelets by Automated Methods", significant time interval restrictions were proposed for Platelet collection during collection of single product, double product and triple product apheresis platelets since studies observed a sustained decrease in platelet counts among plateletpheresis donors at all frequencies of donation , most marked decrease noted in the most frequent donor sections. The time interval between successive apheresis platelet donation intervals for single product collection should be atleast 48 hours (2 days); for double product collection was a 7 day interval and a triple product collection was 14 day period interval.[42]

AABB standards set the maximum blood donation at 10.5 ml/kg. The Council of Europe (CoE) guidelines sets the maximum blood donation at not more than 13% of total blood volume. Most of the clinicians and blood bankers used 70 ml/kg as a rough estimate of blood volume and to determine the lowest acceptable donor weight. Also, it was observed that the 70 ml/kg approximation was found to be an imprecise method to estimate the blood volume, especially for small blood donors. Hence, it is preferable to use formulas that consider individual's sex, height, weight for calculating donor's total blood volume.[43]

According to the UK Guidelines for Blood Transfusion services, 2005, the following guidelines were established, namely, viz.,

(a) First-time apheresis donors should have given at least one routine blood donation without untoward effect within the last two years as this may give an indication of their ability to tolerate an apheresis procedure.[44]

(b) The minimum weight for the apheresis donors should be 50 kg.[44]

(c) The predicted post procedure platelet count should not be < 100 x 10^9/L.[44]

(d) For all types of donor apheresis procedures, mandatory screening tests must be performed at each donor attendance.[44]

(e) In addition the platelet count should be performed at each visit for plateletpheresis donors.[44]

(f) The full blood count must be carried out at least annually for all donors and serum albumin and total serum proteins must be measured at least annually for plasma donors.[44]

(g) A system must be in operation for regular review of these results, together with a documented protocol of the action to be taken in the light of any abnormal findings.[44]

(h) In any apheresis unit, or at any blood donor session where apheresis is performed, a telephone must be immediately available so that the emergency services can be called at any time.[44]

(i) The consultant with responsibility for apheresis must ensure that, as a minimum requirement, all healthcare professionals involved with apheresis procedures receive basic life support training annually.[44]

(j) Resuscitation equipment as required by local and National Guidelines for blood donor sessions must be available at all sessions undertaking routine apheresis procedures. [44]

(k) ECV is the total volume of blood and plasma removed from the donor at any time. It includes all blood and plasma in collection packs and contained within the machine harness (volumes contained within collection harness can be obtained by reference to manufacturers' manuals). Anticoagulant ratio during collection influences the volume of anticoagulant in collected plasma. [44]

Various country wise guidelines are available regarding the limit of extracorporeal volume that needs to be allowed for an apheresis donor during each apheresis procedure. They are summarised below as follows

Table 1: Guidelines on Limit of Extracorporeal volume across various countries

Source	France[81]	UK[44]	Germany[82]	European guidelines[81]	US/FDA[58]	US/AABB guidelines[45]
Extracorporeal volume (ECV) definition	None	Total volume of blood and plasma removed from the donor at any time. It includes all blood and plasma in collection packs and contained within the machine harness.	None	None	None	Donor intravascular volume at all time.
Total Blood Volume (TBV) definition	None	70 ml/kg x donor weight	None	None	None	BV (Males) = 2740 ml/m^2 BV (Females) = 2370 ml/m^2
ECV limit	20% of TBV	20% of TBV excluding AC	15% of TBV	20% of TBV	None	10.5 ml/kg
Maximum product volume	600 ml excluding AC	15% of TBV excluding AC	650ml excluding AC	600 ml excluding AC; 650ml including AC. (Note: these limits can be exceeded if a suitable form of fluid replacement is provided)	500 ml excluding AC for donor wt. <175 lb; 600 ml excluding AC for donors wt. >175 lb.	None
Control of citrate reinfusion rate	None	0.015 mmol/Kg/min	None	None	None	None

CARE OF APHERESIS DONORS

Care of apheresis donors involves 3 major steps, namely, viz.,

I. Preparation of the donor

II. Completion of the procedure

III. Post donation care of the donor[46]

I. Preparation of the Donor

Informed written consent should be obtained from the donor after providing general explanation of the procedure, possible risks and side effects involved during the procedure, expected duration and disclosure of testing done to prevent transmission of diseases by transfusion. [46]

(a) Vein selection

The importance of proper vein selection and phlebotomy technique is to minimize discomfort and risks to donor, to ensure an adequate blood flow and to reduce possibilities of incomplete collection. Antecubital fossa is the most common site for phlebotomy. One (or) more suitable veins are chosen for single or dual arm procedures respectively. Donors can indicate preferences of arm band on comfort (or) successful use in previous donation. A tourniquet is placed above the elbow and the donor will engorge the vein by fist closing motions to facilitate venipuncture.[46]

(b) Preparation of arm

Needle insertion site and the skin surrounding it should be aseptically prepared by mechanical cleaning with application of chemical disinfectant

(chlorhexidine/iodine) according to standard operating procedures. This helps in reducing the size of bacterial contamination. It is important to ensure that the donor is not allergic to chemical disinfectant used. The cleaned site should not be touched after the arm scrub is performed.[46]

(c) Phlebotomy

Most of the apheresis kits contain a pre-attached 17-gauge needle for phlebotomy. [46]

II. Completion of procedure

(a) Separation of blood and collection of products:

Once venous access is established, plateletpheresis procedure can be started. It is important to enter the donor's height, weight, haematocrit and platelet count required by the plateletpheresis device to optimise the procedure for the donor and the products being collected. The donors are made comfortable with entertainment (TV or Music) to divert their attention. Plateletpheresis personnel who are attentive, confident, reassuring and knowledgeable are key to a successful donation that will minimize adverse events. [46]

(b) Prevention and Management of Donor Reactions:

Most plateletpheresis procedures are completed without most significant adverse effects, although inherent risks exist for each and everyone. Implementation of practices that minimise adverse reactions and training of personnel to recognise and properly treat adverse reactions should be the major responsibility of donation centres. Plateletpheresis donation centres should have written procedures to assess

investigate and monitor adverse effects. Proper documentation of type and severity of the reactions, treatment given and status of donor post intervention are important. Contacting the donor after significant adverse reactions and follow up, not only provides important data, but paves the way for a good customer service. Compared to whole blood donations, the overall rate of adverse events in plateletpheresis donation is approximately 10 times less and the mild reactions outnumber the more severe reactions. Hospitalisation is extremely rare with 0.01% incidence in one study. [46]

❖ **Hypotensive Reactions**

Hypotensive reactions can be due to intravascular volume depletion, vasovagal reactions, citrate toxicity, severe allergic reactions and air embolism. Of these, the most common are vasovagal reaction and citrate toxicity. Hypovolemia is uncommon as a result of limitations on extracorporeal volume (allowable upto 10.5 ml/kg). Air embolism is extremely rare because of air detectors on all current instruments. [46]

Sympathetic activation induced by mild hypovolemia results in excessive parasympathetic activation in the donor which leads to signs and symptoms of vasovagal reactions (light headedness, hot flushes, pallor, diaphoresis, nausea, vomiting, reduced heart rate, reduced BP). Since sympathetic activation has a psychological component, it is important to make the donor (especially the 1st time apheresis donor) feel comfortable and confident throughout the procedure. Treatment of vasovagal reactions includes pausing the procedure, lowering the head and raising the feet of donor (Trendelenburg position), applying cold compresses to

neck and forehead, reassuring the donor. In case of moderate/severe symptoms, the procedure should be discontinued. Infusion of intravenous fluids and return of remaining blood within the extracorporeal circuit should be considered. [46]

❖ **Haematoma formation and infiltration**

Complications of venous access can occur at any time during the procedure. The possible acute complications include haematoma formation, infiltration and thrombosis. Symptoms include pain, pressure and bruising or swelling at the needle site. Failure in venous access can lead to abandoning the procedure and the donor's physical discomfort can influence his/her decision about future donation. [46]

Treatment includes discontinuing the collection, removing the needle, cold compress to the injured site. The major risk factor for this reaction is the inexperienced phlebotomy staff. [46]

Preventive strategies include ensuring competency of the plateletpheresis personnel and encouraging donors to be well hydrated before the procedure. It is important to instruct the donor to keep the needle site secure and stable during donation. [46]

❖ **Loss of consciousness and seizures**

It is uncommon and usually due to vasovagal reactions or severe toxicity. Donor may experience tonic-clonic jerking, but this is not true seizure. Very rarely, true seizures can occur following severe citrate toxicity or from an underlying donor seizure disorder. In such cases, procedures should be discontinued immediately. [46]

III. Post Donation Care

(a) Discontinuation of the apheresis procedure

At the end of the collection, blood remaining in the circuit is returned to the donor. Needles are then removed and pressure is applied to the venipuncture site till the bleeding is stopped. A pressure dressing is applied to the phlebotomy site. [46]

(b) Post donation instructions

The following post donation instructions are provided to the apheresis donor upon completion of the procedure, namely, viz.,

- encouragement to leave the bandage in place for a specified interval
- avoiding strenuous activities (lifting/pulling arms for particular time)
- To eat well and drink plenty of fluids for next 24 hours
- To avoid smoking and alcohol, since smoking induces hypotension
- Instructions about action to be taken if venipuncture site begins to bleed
- Educational material about bruising and healing of phlebotomy site
- Contact particulars in case of any occurrence of adverse reactions after leaving the donation area for the donors to notify. [46]

(c) Release of donors

Once the donors are feeling well, they are asked to stand by the chair for a few moments to ensure that they do not have hypotension. They are then escorted to the donor lounge for refreshments. After this, they are observed for atleast 15 minutes for any adverse reactions. If the donor is feeling comfortable, then they are allowed to leave the donation centre. [46]

ANALYSIS OF PARAMETERS

Biochemical Parameters

Plateletpheresis technique requires infusion of citrate into the system to prevent clotting of extracorporeal blood collected in the apheresis circuit. Hypocalcemia due to citrate anticoagulation is the most frequently encountered apheresis specific reaction. Citrate anticoagulation also affects total magnesium levels. Although hypocalcemia induced symptoms are mild in nature, the citrate infusion has got the potential to cause severe donor injury by progressing to frank tetany with spasm in other muscle groups including life – threatening laryngospasm, Q-T prolongation and fatal arrhythmias.[10]

Hypocalcemic reactions are more common among platelet donors (12%) as compared to plasma (5.9%) or granulocyte donors (9.4%). Studies state that 16-50% plateletpheresis donors develop citrate related reactions. [10]

In a study conducted in a tertiary college hospital, it was observed that the mean total calcium levels had a significant (P value < 0.05) continuous and gradual fall from baseline till the end of the procedure (9.83 ± 0.64 mg/dl vs 8.33 ± 0.78 mg/dl) but levels reached near their baseline values (9.42 ± 0.54 mg/dl) after 30 minutes of completion of the procedure. Similar observation was seen with magnesium levels (2.36 ± 0.3 mg/dl vs 1.39 ± 0.40 mg/dl; baseline level: 2.25 ± 0.25 mg/dl). [10]

Certain studies reported a modest and not significant fall in total calcium and total magnesium but a statistically significant fall in ionised calcium and ionised magnesium. It was observed that in procedures performed without prophylactic

calcium supplementation, ionised calcium levels decreased upto 35% as against 20% observed with prophylactic calcium supplementation. Clinically significant citrate related complaints were observed in more than 50% of apheresis procedures. Hence, plateletpheresis procedures are very safe for donors with only a very small percentage (0.89%) were being affected with severe adverse reactions. Understanding the risk factors and aetiologies of adverse donor reactions are very important in protecting donor safety and retaining the plateletpheresis donors. [10]

Administration of oral or intravenous calcium in association with citrate infusions provides enhanced level of donor comfort permitting increased component yields. Bolan *et al* recommends administration of 2g of oral calcium carbonate approximately 30 minutes before donation to counter significant citrate- related adverse effects associated with plateletpheresis procedure.[10, 12]

In a study conducted in a deemed medical college hospital, it was observed that there was a significant decrease in serum magnesium levels after the plateletpheresis procedure as compared to the pre-procedure level (2.43 mg/dl vs 2.16 mg/dl). Hypomagnesemia is observed with both hypocalcemia and hypokalemia. Hence, hypomagnesemia leads to increased intracellular calcium level and thus decreased plasma calcium level. In another study by D.Mercan *et al*, it was observed that an acute and steep drop in ionised magnesium was observed following citrate administration.[47]

In a study conducted on 20 plateletpheresis donors performed on two different cell separators – Baxter CS 3000 and Haemonetics MCS 3p,it was observed that there was an initial, non- significant drop in tCa^{2+} in both the

machines. The mean tCa^{2+} fell from 2.62±0.12 mmol/L to 2.36±0.12 mmol/L and mean tMg^{2+} fell from 0.89±0.1 to 0.79±0.01 mmol/L. There was a statistically significant decline in iCa^{2+} levels (1.33±0.1 mmol/L vs 0.84± 0.1 mmol/L) and iMg^{2+} levels (0.53±0.01 mmol/L vs 0.35±0.1 mmol/L). However, no donor adverse reactions were observed during the study.[33]

In a study conducted on 7 healthy donors undergoing three 90-minute plateletpheresis procedures at continuous, fixed citrate infusion rates of 1.1, 1.4 and 1.6 mg/kg/min, it was observed that total calcium decreased by 3% but there was no significant change observed in total magnesium at the end of the procedure. During plateletpheresis procedures, the findings are suggestive that, whenever there is an increase in citrate infusion rate > 1.0 mg/kg/min, there will be an increase in donor symptoms associated with increased citrate levels.[48]

Haematological Parameters

In a study on 457 healthy first time plateletpheresis donors conducted on five different apheresis systems, it was recommended that apheresis donors should be examined for post donation drop in various haematological parameters with low normal pre-procedure platelet counts (150-200 x 109/L) and Hb concentrations (12.5-13 g/dl). Also, it was suggested that donors with significant decrements should be reviewed subsequently to exclude or, if necessary to treat iatrogenic anaemia and thrombocytopenia.[9]

In a study conducted on 265 plateletpheresis donors, transient but significant decrease in CBC values (87% drop for WBC, 89% drop for Hct & Hb, 100% drop

for platelet count) have been documented but were not high enough to cause clinical problems for plateletpheresis donors.[49]

In a study conducted on 11,464 apheresis collections from 939 donors, it was observed that regular plateletpheresis donors developed sustained decreases in platelet count, but clinically significant thrombocytopenia was unusual.[20]

In a study on 51 plateletpheresis donors performed on three cell separators to find out the best multicomponent apheresis machine, it was observed that MCS+ demonstrated the greatest efficiency in leukodepletion with its integral filter as compared to the Amicus and Trima Accel.[23]

Procedural Parameters

Standard citrate infusion rates exist for plateletpheresis procedures leading to equitable redistribution and metabolism of infused citrate into the plateletpheresis donors. Shorter duration of procedure prevents accumulation to toxic levels whereas longer and repeated procedures lead to citrate accumulation outpacing the metabolism of citrate resulting in markedly decreased ionised calcium levels and significant donor symptoms. A higher citrate infusion rate leads to greater processed volumes and component yields with faster processing rates but were accompanied by progressive decrease in ionised divalent cation levels as serum citrate increases.[10, 48]

Blood processing rates during a plateletpheresis procedure are determined by venous access in addition to citrate toxicity that develops in the donors. Anticoagulant toxicity occurs more frequently in the 90-110 pound (41-50 kg)

donors, if usual blood processing rates (50-70 ml/min) are used, because the body size is directly related to the rate at which the administered citrate is metabolised. Inspite of the reduced blood processing rates, a therapeutic dose of platelets can be routinely collected from 90-110 pound donors in a reasonable longer donation time.[50]

Citrate infusion rate is dependent on both the whole blood processing rate and the whole blood to anticoagulant ratio. Adjustments by the operator play a crucial role between occurrence of donor symptoms and collection of effective platelet yield.[12]

Platelet yield of the collected product have an important economic effect on platelet apheresis programme. In a study on 5780 products collected through two different cell separators, it was observed that an increase in baseline donor platelet count by recombinant thrombopoeitin therapy decreases the apheresis cost for each single donor by 30%, from USD 378 to USD 267 per unit.[51]

ADVERSE EVENTS DURING PLATELETPHERESIS PROCEDURE

The safety of the donor is a major concern during plateletpheresis procedure. The duration of plateletpheresis procedure and its relative complexity in comparison to the standard phlebotomy has led to the perception of ‘increased donor risk’. However, in plateletpheresis procedure, the red cells are not depleted and the volume lost is replaced with intravenous solutions leading to fewer incidences of hypovolemic reactions compared to whole blood donation. Though studies on plateletpheresis donors emphasized mild and transient citrate effects especially

paresthesias in substantial proportion of donors, it has been concluded that plateletpheresis procedure is a safe and well tolerated procedure.[52]

First time whole blood donors are known to have more adverse effects as compared to the repeat donors, especially vasovagal reactions and the same is applicable for first time apheresis donors. In a study conducted across 17 centres, there was a lower rate of non venipuncture adverse events. Such events were mainly seen in first time donors, donors receiving higher citrate infusion rates and anticipated greater extracorporeal volume depending on the type of cell separator used.[52]

It was also observed that apheresis is a safer procedure as compared to whole blood donation in terms of occurrence of adverse events, since the longer time duration of the procedure allows better fluid equilibration and lower risk of hypovolemia or syncope.[22]

Donor adverse reactions are broadly grouped into two categories – Immediate reactions or Delayed reactions. Sex, Race/ethnicity, donation site and donation history are significant contributors to delayed reactions. Pre-donation donor blood volume is inversely associated with likelihood for development of either immediate reaction or delayed reaction.[43]

- ***Citrate toxicity***

The transient hypocalcemia associated with apheresis is usually well tolerated; nevertheless, certain physiologic consequences may be encountered. Decreases in ionised calcium can increase the excitability of nerve cell membranes,

reducing the threshold for neural impulse triggering and resulting in spontaneous depolarization. This usually manifests as mild perioral and/or peripheral paresthesias (ie, tingling sensation). A smaller proportion may experience dysgeusia (unusual taste), nausea, and/or light headedness. Shivering, twitching, and tremors are rare but have been reported. Prompt identification of mild symptoms during plateletpheresis procedures requires only temporary pausing or stopping the procedure to reduce the reinfusion rate and thus prevent severe citrate reactions.[31]

Sequelae of citrate toxicity depends on the (a) rate of citrate administration; (b) duration of citrate infusion; (c) dilution of citrate in the ECF ; (d) redistribution; (e) rate of metabolism and finally (f) rate of excretion of citrate. Experimental studies have shown a rapid initial citrate clearance of 50% over the first 30 minutes followed by gradual clearance of remaining 50% over the next 2 ½ hours. The citrate level in serum and urine typically returns to baseline within 4 hours after stoppage of infusion.[31]

Symptoms of citrate toxicity are rarely seen at citrate infusion rate of 1 mg/kg/min. However, when rates exceed 1.7 mg/kg/min, donors are associated with risk of developing moderate to severe citrate reactions. In addition, the size of the donor affects citrate accumulation. At a similar citrate infusion rate, smaller donors experience acute symptoms of citrate toxicity at greater frequency as compared to larger donors due to less ECF available for dilution of citrate and a lesser mass of tissue to metabolise the compound. Reiterating the above facts, in another study done on 12 plateletpheresis donors, it was observed that low body weight, high citrate level and low ionised calcium were associated with hypocalcemic symptoms.[24, 31]

Increase in citrate infusion rate increases the total volume processed and the platelet yield but also has been observed to increase the severity of donor symptoms. A rapidly continuous increase of serum citrate levels occur during plateletpheresis procedures in healthy donors leading to increased citrate levels which are associated with mean peak reductions of upto 33% in iCa and 39% in iMg at the end of the procedure. Whenever higher citrate infusion rates are used in lighter weight donors, during plateletpheresis procedures, administration of oral or intravenous calcium in association with citrate infusions provides a greater level of donor comfort and permits increased donor yields.[48]

Citrate infusion is invariable in plateletpheresis donations and hence the mild tingling sensation is accepted both by donors and blood collection personnel as a manageable and harmless reaction. During earlier periods, intermittent flow centrifugation procedures were followed. In these, citrate was infused intermittently but at a high flow rates. Later, instrument designs and procedure specifications ensured lower and constant citrate infusion rates, even in intermittent flow instruments, thus reducing the incidence and severity of citrate effects.[52]

Mild citrate related toxicity that occurs following plateletpheresis procedure was attributed to the larger amount of ACD used and was successfully treated by reducing the ACD infusion rate, the amount of ACD used and/or oral calcium supplementation.[53]

According to guidelines issued by BCSH on the clinical use of apheresis procedures, hypocalcemic toxicity can be significantly ameliorated by reducing the rate of citrate delivery and overall procedure time and/or by prophylactic

administration of calcium. Also, it states that mild citrate toxicity is a common adverse event of apheresis and the transfusion service may seek to reduce its incidence through measures such as prophylactic oral or IV calcium.[84]

According to guidelines issued by BCSH on the clinical use of blood cell separators, oral calcium supplements can be given either before or during the procedure to prevent development of hypocalcemia.[85]

- ***Vasovagal reactions***

Few hospitals in the city have been exposed to the utilisation of apheresis technology for collection of specific blood components. This results in first time apheresis donors coming into the apheresis setup with a lot of apprehension.[13]

Pathophysiology model of Vasovagal Syncope

The pathophysiological model of vasovagal syncope was first described by Edward P Sharpey-Shafer of St.Thomas Hospital in London. Blood pooling as a result of upright posture leads to relative central volume depletion and reduced cardiac preload resulting in gravity dependent vasovagal syncope. For maintenance of blood pressure, a baroreceptor mediated increase in sympathetic nervous system tone, with a resultant increase in cardiac contractility. The high contractility combined with under-filled ventricles is sensed as excessive by cardiac mechanoreceptors. This leads to baroreceptor mediated sudden increase in parasympathetic tone and withdrawal of sympathetic tone. Vasovagal syncope patients experience bradycardia or periods of asystole, and/or vasodilatation or venodilatation. The common triggers for occurrence of vasovagal syncope includes

prolonged standing (upright posture) or sitting; activation of large muscles via reduction in cardiac preload. Cortical triggers such as anxiety, severe emotion or pain also triggers vasovagal response, probably due to direct actions of medulla.[54]

Factors that are independently associated with significant hypotensive reactions in plateletpheresis procedures include gender, weight, harvesting of plasma, frequency of donation and other citrate related symptoms (e.g. paresthesia). Hypotension during apheresis donation can be due to hypovolemia but citrate toxicity can also independently lead to hypotension and in those patients, symptoms of paresthesia, nausea were the most significant independent predictor of hypotension related to citrate toxicity. Hypotension related to citrate toxicity is due to hypocalcemia related vascular smooth muscle relaxation, depressed myocardial function and arrhythmias with prolonged QT intervals. So, it is recommended to check BP in all donors who have citrate related symptoms that are recurrent /resistant to palliative treatment. Position of tubing within the apheresis machine roller pump mechanism should be carefully monitored. Hypotension due to citrate toxicity can be prevented either by supplementation of oral calcium prior to platelet donation or by following a step down protocol for ACD – A anticoagulant solution resulting in significant reduction in the quantity of citrate injected.[55]

Vasovagal reactions are characterised by pallor, sweating, nausea, hypotension, fainting and loss of consciousness.[56]

The minimum accepted weight for persons to donate blood in the United States is 110 pounds (50 kgs). During the process of whole blood donation, the donor experiences a sudden, fixed (usually 450-470 ml) loss of blood volume that is

slowly corrected only by normal physiological mechanisms. In contrast, during plateletpheresis procedures, the donor is maintained in a positive fluid balance state throughout the course of the donation due to administration of priming solution, use of anticoagulant solutions and use of fluid to return the donor cells at the end of the procedure. Due to the above factors, donors donating platelets gain volume rather than lose it, as a result of apheresis procedure.[50]

In a multi-centre study conducted across two Italian transfusion centres on 2641 plateletpheresis donations, the overall adverse event rate among plateletpheresis donations was 7.84%, with the most common adverse event being vasovagal reaction of mild severity followed by mild citrate toxicity. None of the adverse events noted belonged to severe category and all the mild adverse events responded adequately with corrective measures emphasizing the safety profile of plateletpheresis procedures.[57]

Hypotensive reactions after blood donation are typically vasovagal in nature. Physiologic responses to orthostatic changes and hypovolemia play a role in determining reaction rate and severity. The primary stimulus for vasovagal reaction is psychological with mild hypovolemia predisposing to syncope. Clinical symptoms of blood loss upto 15% of total blood volume are minimal. However, blood volume loss in the range of 15-30% (Class II haemorrhage) is associated with tachycardia, tachypnea, decrease in pulse pressure and subtle central nervous system changes in the form of anxiety.[43]

Gender plays a role in the occurrence of vasovagal reactions. Compensation for acute hypovolemia and hypotension varies with sex. Systemic BP is regulated by

a process which involves musculature, venous valves, autonomic nervous system, and renin-aldosterone-angiotensin system (RAAS). Estrogen upregulates angiotensinogen, but down regulates renin, angiotensin converting enzyme, and angiotensin II Type 1 receptor, with a net effect of suppression of RAAS. In contrast, testosterone increases angiotensinogen mRNA and plasma renin activity and leads to blunting of pressure – natriuresis relationship, controlled by RAAS In normotensive human volunteers, females have lower baroreflex sensitivity than males suggesting that cardiac vagal component seems to play a smaller role in baroreflex mediated bradycardia in females. Also, orthostatic tolerance was lower in females under hypovolemic conditions, predominantly due to smaller stroke volume which is due to reduced cardiac filling. [43]

Fainting during or immediately after completion of a collection procedure may be neurocardiogenic (vasovagal), while fainting more than 10 minutes after donation may be related to orthostatic intolerance exacerbated by hypovolemia of blood donation. [43]

- ***Hematoma formation***

In a study conducted on nearly 19,611 responses from 17 centres concerning 250 to 2,000 consecutive apheresis procedures per centre, the overall adverse event reported was 2.18% of donations and the most common among these were the venipuncture related complications with 1.15% of donations followed by non – venipuncture related complications which were 1.04% of donations. Venipuncture related complications were more common among first time donors as compared to repeat donors with female gender being more commonly affected as compared to the

male counterpart. The reason attributed was to the thin & fragile nature of veins seen in female donors as compared to the male donors.[52, 55]

Haematoma formation usually occurs during initial stages when plateletpheresis procedures are being established probably due to untrained staff in handling the apheresis needle which is in slight modification to the regular whole blood donation needles.[6]

Materials & Methods

MATERIALS AND METHODS

Study design

This study is a Cross sectional study conducted in the Department of Transfusion Medicine, The Tamil Nadu Dr.MGR Medical University, Guindy, Chennai and the Blood Bank, Adyar Cancer Institute (WIA), Adyar, Chennai and was approved by the respective Institutional Ethical Committee.

Study population

Study population includes voluntary blood donors who fulfilled the eligibility criteria for plateletpheresis donation as per the guidelines of Directorate General of Health Services (DGHS) in the Department of Transfusion Medicine, The Tamil Nadu Dr.MGR Medical University, Guindy, Chennai and in the Blood Bank, Cancer Institute, Adyar during the study period from July 2016 to August 2017.

Inclusion criteria

All voluntary blood donors (preferably donated whole blood at least 1-2 times earlier) are selected according to guidelines issued under Directorate General of Health Services (DGHS) standards.

Exclusion criteria

- All blood donors who do not fulfil the inclusion criteria as stated above are excluded.
- Blood donors who are not willing to participate in the study are excluded.

Informed consent

All study details will be explained and written informed consent obtained from the blood donors in either English language or in local vernacular language (whichever is preferred by the donor) who visit the Department of Transfusion Medicine, The Tamil Nadu Dr.MGR Medical University, Chennai and the Blood Bank, Cancer Institute, Adyar.

Sample size

Sample size was calculated using nMaster software using the formula:

$$N_{pairs} = \frac{\left(z_{1-\alpha/2} + z_{1-\beta}\right)^2}{\Delta^2} + \frac{z^2_{1-\alpha/2}}{2}$$

$$\Delta = \frac{(\mu_2 - \mu_1)}{\sigma} \qquad \sigma = \frac{\sigma_1 + \sigma_2}{2}$$

Where,

μ_1 : Pre-test mean

μ_2 : Post-test mean

σ_1 : Standard deviation in the pre-test

σ_2 : Standard deviation in the post-test

Δ : Effect size

α : Significance level

1-β : Power

Minimum required sample size : 61

Statistical analysis

Data was entered into MS-EXCEL and statistically analysed using SPSS software Version 20. Demographic details will be given in descriptive statistics. Quantitative data will be given in summary statistics. Pre- and post-procedure

parameters analysed using paired 't' test. Pearson's correlation was used for analysing correlation between variables. $P<0.05$ was considered significant.

Operational definition: (As per DGHS guidelines[2])

A. Donor undergoing an occasional apheresis procedure (performed not frequently than once every 4 weeks) must meet the same criteria as a whole blood donation.

B. Donor should be preferably repeat donor – might have given blood 1-2 times earlier.

C. Written consent of the donor is taken after explaining the procedure in detail, time taken, and about possible hazards and benefits.

D. Venous access is an important consideration in apheresis donor and veins should be examined at the time of the selection of a donor as:

(i) Long needle-in and needle-out times

(ii) Prolonged flow rate

E. Donor should be screened prior to apheresis for markers of infectious diseases transmitted by the transfusion of blood and its components in the same manner as for the whole blood. Each donor must be tested prior to each apheresis unless the donor is undergoing repeated procedures, in such cases testing for markers of diseases need to be repeated at 30 days interval.

F. Tests for haemoglobin, ABO group, Rh type, and screening for unexpected antibody are done.

G. More stringent regulations govern the donor who participate in the serial apheresis program (procedure performed more frequently than 4 weeks)

(i) Interval between two procedures should be atleast 48 hours and the loss of red cells should not exceed 25 ml per week.

(ii) If donor's red cells could not be reinfused during a procedure, or if a participant donates a unit of whole blood, 12 weeks should elapse before subsequent apheresis procedure.

- Age should be between 18-50 years.
- Weight be 60 kg or more
- Haemoglobin: 12.5 g/dl or more.

H. Donors who have taken aspirin containing medication within 36 hours are usually deferred.

I. Platelet may be collected from donors who do not meet the requirement if the component is of particular value to the patient – HLA matched donors.

J. The interval between procedures should be atleast 48 hours. A donor shall not undergo the procedure more than 2 times in a week or 24 times in a year.

K. If plateletpheresis is performed more frequently than every 4 weeks, a platelet count should be done and must be more than 150,000/µl prior to performing subsequent plateletpheresis.

L. The platelet count may be done before all plateletpheresis so that donor's health is not compromised.

METHODOLOGY

- Voluntary blood donors who arrive at the blood bank are offered pre-donation counselling and provided information regarding the details of the plateletpheresis procedure with its relative consequences and willingness to donate Single Donor Platelet confirmed.

- Informed written consent is obtained from the voluntary blood donor in the Apheresis Donor Questionnaire form and the Proforma form for study purpose.

- Voluntary Blood Donor is allowed to fill up the Apheresis Donor Questionnaire Form and physical examination including the basic demographic profile of the donor is performed by the investigator.

- In our study, the apheresis donors were given prophylactic calcium supplementation through intravenous and oral administration in order to ameliorate symptoms of hypocalcemic toxicity.[84]

- All eligible plateletpheresis donors (n=63) are divided into two groups – One group of 32 donors given 1 tablet (125mg elemental calcium) of oral calcium supplementation before the start of the procedure and another group containing 31 donors given 1 ampoule (10 ml of 10% Calcium gluconate - 0.931% calcium) of intravenous calcium infusion drip with normal saline. For the oral calcium supplementation group, additional calcium tablets were given whenever the donors complained of symptoms of hypocalcemia due to citrate toxicity.[85]

- Donors are classified according to WHO guidelines on BMI distribution[69] as follows

Table 2: BMI Distribution – WHO Classification

S.No.	BMI Distribution	Category
1.	< 18.50	Underweight
2.	18.50 – 24.99	Normal
3.	25.00 – 29.99	Overweight
4.	30.00 -34.99	Obese Class I
5.	35.00 – 39.99	Obese Class II
6.	≥40.0	Obese Class III

Sample collection & testing

- Sample for analysis was collected from the arm that was not utilised for the plateletpheresis procedure.

- 5 ml (Five) of whole blood from each donor was collected as follows – 2 ml (Two) into ethylene diamine tetra acetic acid (EDTA) contained lavender coloured vacutainer tubes and 3 ml (Three) of whole blood into plain red topped vacutainer tubes just before and within 30 minutes after the completion of the plateletpheresis procedures.[78,79]

- Both the vacutainer tubes were thoroughly mixed and placed in a stand.

- The red topped tubes are allowed to clot and the serum separated from the red cell clot within 2 hours of collection and values measured. [78,79]

- ABO Blood grouping and Rh typing of donor sample was done.

- Screening for Transfusion Transmissible Infections was done on donor's sample using rapid screening kits prior to donation and later (post donation) , the sample was tested by ELISA technique.[83]

- Haematological parameters of the donors were analysed using calibrated automated cell counter – Mindray BC 5380 and biochemical parameters analysed using calibrated automated biochemical analyser - COBAS C311 (Roche Diagnostics).

- Once the screening profile is negative for TTIs and the eligibility criteria fulfilled according to guidelines issued under DGHS Standards, Technical Manual, 2003, the donor is subjected to plateletpheresis procedure.

- Baseline values of all haematological and biochemical parameters are noted in the Proforma sheet.

- All plateletpheresis donations were performed using Haemonetics MCS+ apheresis machine (Haemonetics Corporation, Braintree, MA, USA), a single needle procedure following the principle of intermittent flow centrifugation and fluid surge elutriation.

- Preparing the MCS+ device involves inserting the LDP protocol card and closing the card port door securely.[80]

- Once, the power is on, the device runs a self diagnostic testing. [80]

- After the self test, protocol options for LDP and volume compensation for the donor using saline solution are selected. [80]

- The disposable kit is installed in a sequential manner as per the instructions displayed in the 'Initial Installation Screen Display'. [80]

- After proper installation, visual inspection of the disposable kit as per the 'Pre-pump autoload screen display' instructions are performed and completion of action ensured. [80]

- Pump autoload sequence is initiated and instructions issued as per the 'Pre-priming screen display' are ensured. [80]

- The anticoagulant solution (ACD-A) and the normal saline solution are spiked in the corresponding ports and priming of LDP disposable kit are performed using the anticoagulant solution as per the manufacturer's instructions. [80]

- On completion of the priming sequence, 'Haemo-Calculator' page is displayed, in which the following details are manually entered for the procedure to initiate: Sex (Male/Female), Height (cm), Weight (Kg), Haematocrit (%), and Pre-platelet count (x 10^3/µL). [80]

- The endpoint for the product collected was fixed with the target yield of 3 x 10^{11} platelets per unit. [5]

- Blood flow rate for all collections was maintained within apheresis device manufacturer's recommendations (Draw rate maintained @80 ml/min with

return rate varied between 60-100 ml/min and ACD – A anticoagulant solution in the ratio of 1:9) The values are entered in the Proforma sheet. [80]

- Donor is called into the 'apheresis room' and made to lie in the recumbent (supine) position ensuring that the line of sight is away from the operating area of the device.

- Prophylactic calcium supplementation was given. The entire sample size was divided into two groups – One group of 32 donors given 1 tablet (0.323 g total Ca^{2+}/125mg elemental Ca^{2+}) of oral calcium supplementation before the start of the procedure and another group containing 31 donors given 1 ampoule (0.931% calcium) of intravenous calcium infusion drip with normal saline. For the oral calcium supplementation group, additional calcium tablets were given whenever the donors complained of symptoms of hypocalcemia due to citrate toxicity.[85]

- Cuff is attached to the donor arm after proper selection of the vein. A single, bold venipuncture is performed under aseptic precautions. Initial blood drawn (around 10-15 ml) is collected in the sample diversion pouch, clamped and later the procedure is started as per the manufacturer's instructions. [80]

- Donor is monitored for development of any adverse events and appropriate management protocol followed as per the standard operating procedure.[30]

- On completion of the procedure, the needle line tubing is clamped, cuff released, needle removed under aseptic precautions and the procedural values are noted in the Proforma sheet.[80]

- Post donation, whole blood samples (5 ml) are taken in EDTA (2 ml) and plain red topped vacutainers (3 ml) within 30 minutes from the end of the procedure, samples analysed and results recorded in the Proforma sheet.[78,79]

- Post donation care of apheresis donor is ensured by providing refreshments and ensuring proper hydration. Post donation counselling done for the apheresis donor.[30]

- The following haematological parameters, namely,viz., haemoglobin, haematocrit, RBC count, WBC count, Platelet count, Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) are measured, both before and after the plateletpheresis procedures, their results recorded and correlated with citrate toxicity.

- The following biochemical parameters, namely, viz., serum calcium, serum ionised calcium and serum magnesium levels are measured, both before and after the plateletpheresis procedures, their results recorded and changes analysed with normal reference range for serum calcium (8.9 – 10.1 mg/dL)[88], serum ionised calcium (1.14- 1.38 mmol/L)[89], serum magnesium (1.7- 2.3 mg/dL)[90] and correlated with citrate toxicity. Also, the pre- and post procedural serum ionised calcium levels are analysed with number of oral calcium tablets and with intravenous calcium infusion with normal saline.

- The product SDP bag is allowed a resting period of 1 hour and placing the product bag in platelet incubator cum agitator for atleast 5 minutes before the PC sample is taken.[91]

- A PC sample taken from the product SDP bag was diluted with diluent in 1:4 dilution and the value recorded using calibrated automated cell counter. The product platelet count is arrived by multiplying the value with the dilution factor.[92]

- Actual platelet yield was calculated by using the following formula[22]

Actual Platelet Yield	**=**	**Volume of product**	**x**	**PLT count of PC sample**	**x**	**Conversion factor ($x 10^3/\mu L$)**

- The following procedural parameters namely, viz., number of cycles, Duration, blood volume processed, platelet yield, product platelet volume, return rate , saline used, ACD-A used are recorded at the end of the procedure.

- Based on the pre-procedure platelet count, the following procedural parameters namely, viz., number of cycles, duration, return rate, platelet yield, blood volume processed, ACD-A used are correlated with mild citrate toxicity.

- The occurrence of donor adverse reactions were classified into 4 categories –

  (1) Citrate toxicity due to hypocalcemic symptoms.
  (2) Vasovagal reactions
  (3) Haematoma formation
  (4) Others (arterial puncture, nerve irritation, local allergy, thrombophlebitis)

- Citrate toxicity[46] was further classified into 3 categories as follows

(a) **Mild citrate toxicity** - numbness and/or tingling in lips and nose and sneezing. [46]

(b) **Moderate citrate toxicity** – nausea and/or vomiting; progression to paresthesias to the hands, feet, and/or chest; intense vibrating sensation throughout the body; chills; abdominal cramping; lightheadedness or hypotension. [46]

(c) **Severe citrate toxicity** – painful muscle cramps, tetany, blurred or double vision, loss of consciousness, carpopedal spasm, cardiac arrhythmia and seizure**.**[46]

- Vasovagal reactions[70] was classified as follows
  - (a) Mild reaction – cold extremities, chills, feeling of warmth, hypotension, lightheadedness/dizziness, nausea/vomiting, pallor, slow or rapid pulse, sweating, twitching, weakness. [70]
  - (b) Moderate reaction –MILD symptoms + Loss of consciousness < 60 seconds.[70]
  - (c) Severe reaction –MODERATE SYMPTOMS + Convulsions, Loss of consciousness > 60 seconds, Loss of bowel/bladder control, tetany.[70]
- Presence or absence of haematoma formation was recorded.
- Occurrence of adverse events is entered in the Proforma sheet.

Results

RESULTS

I. Donor Demographic Profile

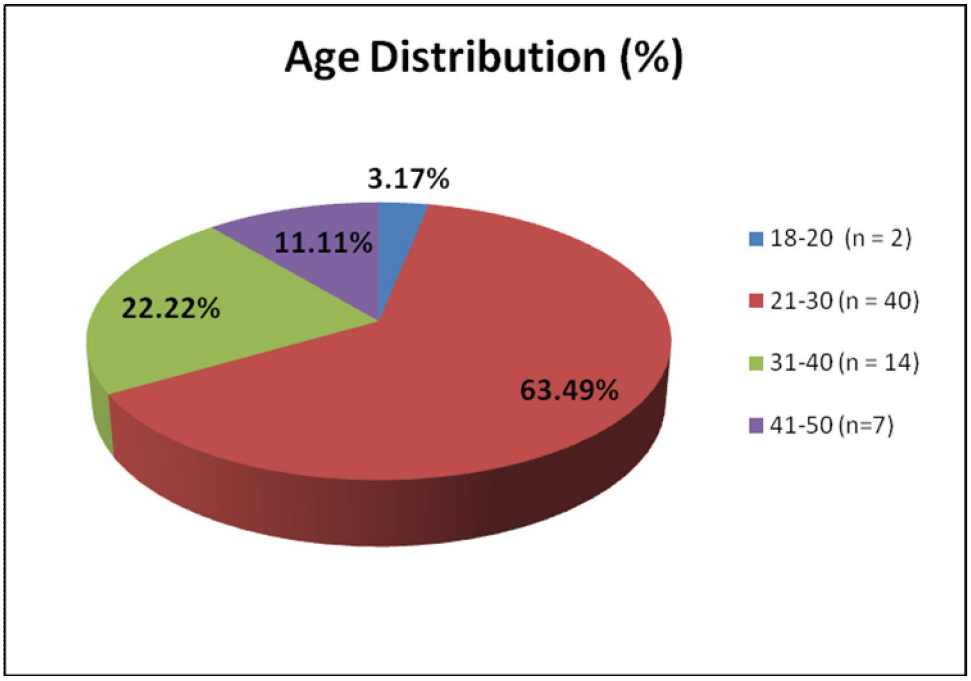

Fig. 4: Age Distribution (%)

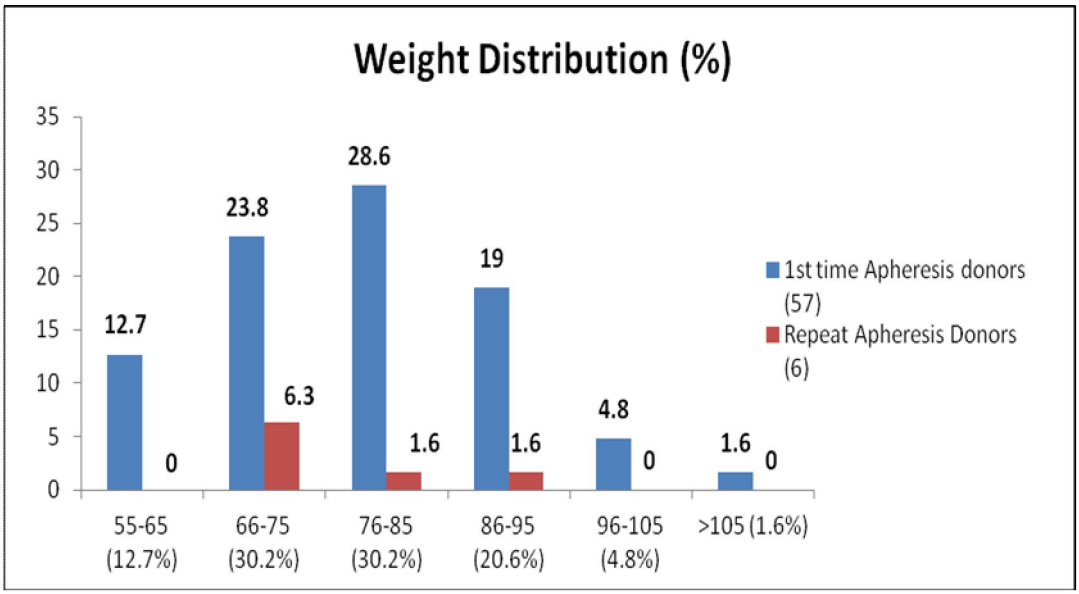

Fig. 5: Weight Distribution among Plateletpheresis donors (%)

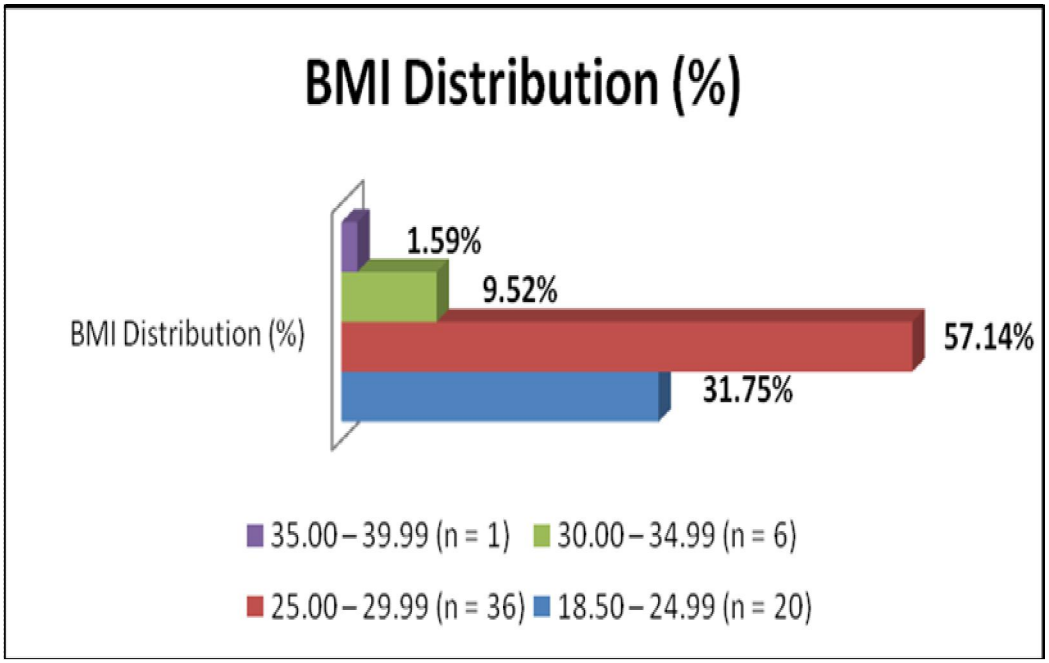

Fig. 6: BMI Distribution (%)

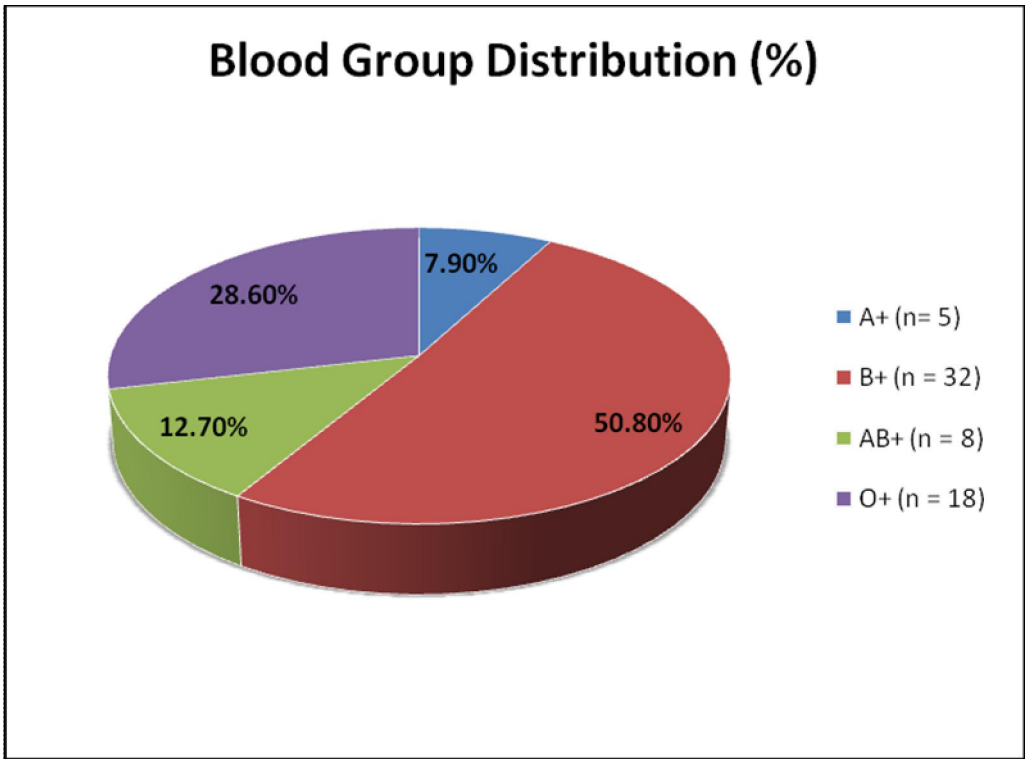

Fig. 7: Blood Group Distribution (%)

Table 3: Sex Distribution

Sex	N	%
Males	63	100 %
Females	0	-

All plateletpheresis donors were males.

Table 4: Donation Status of Plateletpheresis Donors

Donation Status	N	%
1st time apheresis donors	57	90.5%
Repeat apheresis donors	6	9.5%

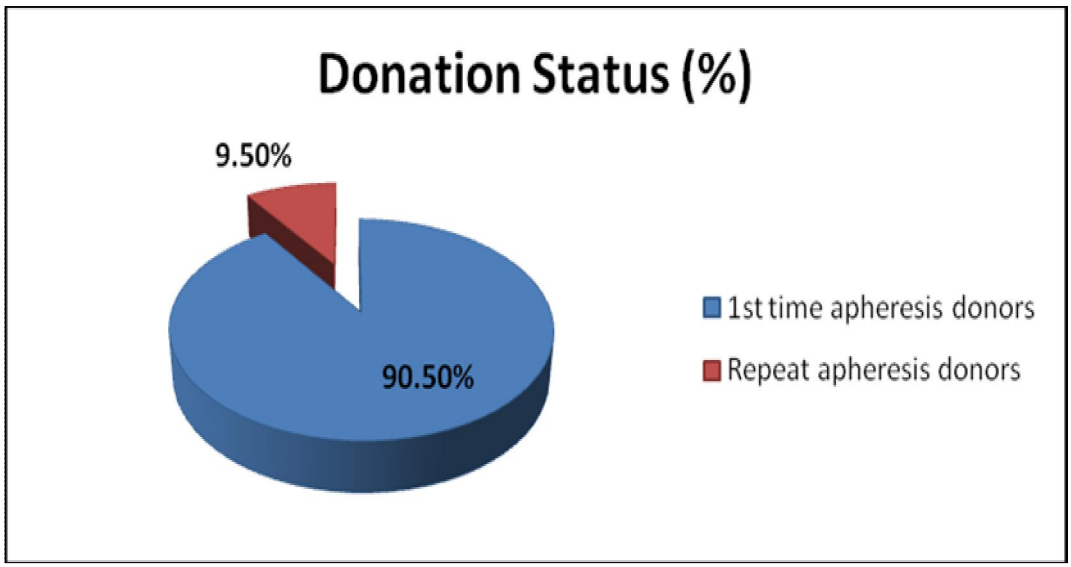

Fig. 8: Donation Status of Plateletpheresis donors (%)

II. Donor Haematological, Bio-chemical & Procedural profile:

Table 5: Haematological values before and after plateletpheresis (n=63)

S.No.	Haemat. Parameter	Pre-procedure (Mean±SD)	Post-procedure (Mean±SD)	Diff. (Mean±SD)	p-value
1.	Hb [g/dL]	14.81±1.24	14.56±1.29	0.25±0.74	**0.009 (<0.05)**
2.	Hct [%]	46.83±4.07	46.33±3.83	0.50±2.25	0.082
3.	RBC Count [x 10^6/µL]	5.09±0.50	5.05±0.51	0.04±0.27	0.239
4.	WBC Count [x 10^3/µL]	7445.56±1740.64	7428.25±1737.66	17.30±684.74	0.842
5.	Platelet count [x 10^3/µL]	263.81±54.50	203.25±47.20	60.56±27.86	**0.000 (<0.05)**
6.	MPV [fL]	9.09±0.90	9.00±0.90	0.09±0.38	0.081
7.	PDW	16.05±0.32	16.10±0.43	(-)0.05±0.30	0.181

(Hb – Haemoglobin; Hct – Haematocrit; RBC – Red Blood Cell; WBC – White Blood Cell; MPV- Mean Platelet Volume; PDW – Platelet Distribution Width)

Table 6: Haematological values before and after plateletpheresis (n=63) – Oral Ca^{2+} group (n=32) and IV Ca^{2+} group (n=31)

S. No.	Haemat. parameter	Mode (Groups)	Pre-proc. (Mean±SD)	Post-proc. (Mean±SD)	Diff. (Mean±SD)	p-value
1.	Hb [g/dl]	Oral Ca^{2+}	15.14±1.26	15.07±1.20	0.07±0.90	0.670
		IV Ca^{2+}	14.48±1.14	14.04±1.17	0.44±0.47	**0.000 (<0.05)**
2.	Hct [%]	Oral Ca^{2+}	46.78±4.66	46.33±4.14	0.45±3.03	0.407
		IV Ca^{2+}	46.88±3.43	46.33±3.56	0.55±1.00	**0.004 (<0.05)**
3.	RBC Count [x 10^6/µL]	Oral Ca^{2+}	5.16±0.52	5.14±0.49	0.02±0.32	0.724
		IV Ca^{2+}	5.02±0.47	4.96±0.52	0.06±0.21	0.116
4.	WBC Count [x 10^3/µL]	Oral Ca^{2+}	7186.56±1773.20	6996.25±1805.29	190.31±715.49	0.143
		IV Ca^{2+}	7712.90±1693.27	7874.19±1570.98	-161.29±612.47	0.153
5.	Platelet count [x 10^3/µL]	Oral Ca^{2+}	267.31±54.68	209.36±54.02	57.94±29.08	**0.000 (<0.05)**
		IV Ca^{2+}	260.19±54.98	196.94±38.84	63.26±26.75	**0.000 (<0.05)**
6.	MPV [fL]	Oral Ca^{2+}	9.01±0.77	8.86±0.75	0.16±0.45	0.058
		IV Ca^{2+}	9.16±1.03	9.15±1.02	0.01±0.29	0.806
7.	PDW	Oral Ca^{2+}	15.99±0.35	16.00±0.49	(-)0.01±0.38	0.927
		IV Ca^{2+}	16.11±0.28	16.01±0.34	0.10±0.17	0.780

(Hb – Haemoglobin; Hct – Haematocrit; RBC – Red Blood Cell; WBC – White Blood Cell; MPV- Mean Platelet Volume; PDW – Platelet Distribution Width)

Table 7: Biochemical parameters before and after plateletpheresis (n=63)

S.No.	Biochemical parameter	Pre-procedure (Mean±SD)	Post-procedure* (Mean±SD)	Diff. (Mean±SD)	p-value (<0.05)
1.	S. Calcium [mg/dL]	10.32±1.47	10.04±0.95	0.28±1.29	0.092
2.	S. i.Ca^{2+} [mmol/L]	1.12±0.19	1.10±0.13	0.02±0.22	0.424
3.	S.Magnesium [mg/dL]	2.13±0.25	2.11±0.20	0.03±0.27	0.423

***-** values after intervention with calcium supplements (both oral and intravenous calcium infusion drip with normal saline)

Table 8: Biochemical parameters before and after plateletpheresis (n=63) - Oral Ca^{2+} group (n=32) and IV Ca^{2+} group (n=31)

S.No.	Biochemical parameter	Mode (Groups)	Pre-procedure	Post-procedure*	Diff.	p-value
1.	S.Calcium [mg/dL]	Oral Ca^{2+}	10.33±1.62	9.88±1.00	0.45±1.35	0.067
		IV Ca^{2+}	10.31±1.33	10.21±0.88	0.10±1.22	0.661
2.	S.i.Ca^{2+} [mmol/L]	Oral Ca^{2+}	1.17±0.09	1.10±0.11	0.08±0.14	**0.003 (<0.05)**
		IV Ca^{2+}	1.07±0.25	1.11±0.14	(-) 0.04±0.27	0.472
3.	S.Magnesium [mg/dL]	Oral Ca^{2+}	2.13±0.30	2.07±0.24	0.05±0.28	0.285
		IV Ca^{2+}	2.14±0.22	2.14±0.14	0.00±0.26	0.995

***-** values after intervention with calcium supplements (both oral and intravenous calcium infusion drip with normal saline)

Table 9: Procedural parameters at the end of plateletpheresis (n=63)

S.No.	Procedural parameter	Actual (Mean±SD)
1.	Duration [min]	81.29±19.24
2.	Blood volume processed [ml]	2689.59±617.4
3.	Platelet yield [x 10^{11}/unit]	3.22±0.85
4.	Platelet volume [ml]	311.86±75.90
5.	Return rate [ml/min]	87.94±12.72
6.	Saline used [ml]	233.71± 97.92
7.	ACD-A used [ml]	283.92±60.05
8.	No. of cycles	6.05± 1.39

Table 10: Procedural parameters at the end of plateletpheresis (n=63) - Oral Ca^{2+} group (n=32) and IV Ca^{2+} group (n=31)

S.No.	Procedural parameter	Oral Ca^{2+} grp.	I.V. Ca^{2+} grp.
1.	Duration [min]	78.53±22.74	83.86±14.87
2.	No. of cycles	5.63 ± 1.58	6.43±0.10
3.	Return rate [ml/min]	86.88±14.91	89.29±10.16
4.	ACD-A used [ml]	266.09±64.93	299.93±50.06
5.	Blood volume processed [ml]	2524.77±578.29	2902.57±457.45
6.	Saline used [ml]	254.71 ± 41.86	275.93±39.60
7.	Platelet yield [x 10^{11}/unit]	3.00±0.78	3.22±0.23
8.	Platelet volume [ml]	282.97±81.24	340.89±47.69

Table 11: Correlation of pre-platelet count with procedural parameters

Pre-procedure platelet count [$x10^3/\mu L$]	**No. of cycles**	**Duration [min]**	**Platelet yield** [$x\ 10^{11}$/unit]
150-200 *(n=9)*	6.89 ± 0.78	91.33± 13.35	3.0 ± 0.00
201-250 *(n=14)*	6.86 ±1. 027	93.07± 15.82	3.0 ± 0.00
251-300 *(n=27)*	5.63 ± 1.57	75.70± 21.05	3.07± 1.29
301-350 *(n=9)*	5.44 ± 0.527	74.44± 10.04	3.22 ± 0.44
351-400 *(n=3)*	6.00 ± 1.73	75.00± 23.52	3.0 ± 0.00
401-450 *(n=1)*	4	57	3.8
P value (Correlation)	**0.000 (r= -0.399)**	**0.001 (r= -0.396)**	**0.022 (r=0.288)**

The pre-procedure platelet count has a negative correlation with number of cycles [r= (-) 0.399] and duration [r= (-) 0.396] and a positive correlation with platelet yield. (r=0.288).

As the pre-platelet count increases, number of cycles and duration decreases with increase in platelet yield.

III. Donor Adverse Reaction profile

Table 12: Distribution of Adverse events among plateletpheresis donors (n=63)

S.No.	Adverse event	N	%
1.	Mild citrate toxicity	26	41.3 %
2.	Vasovagal reaction	3	4.8 %
3.	Haematoma formation	1	1.6 %
Total		**30**	**47.6%**

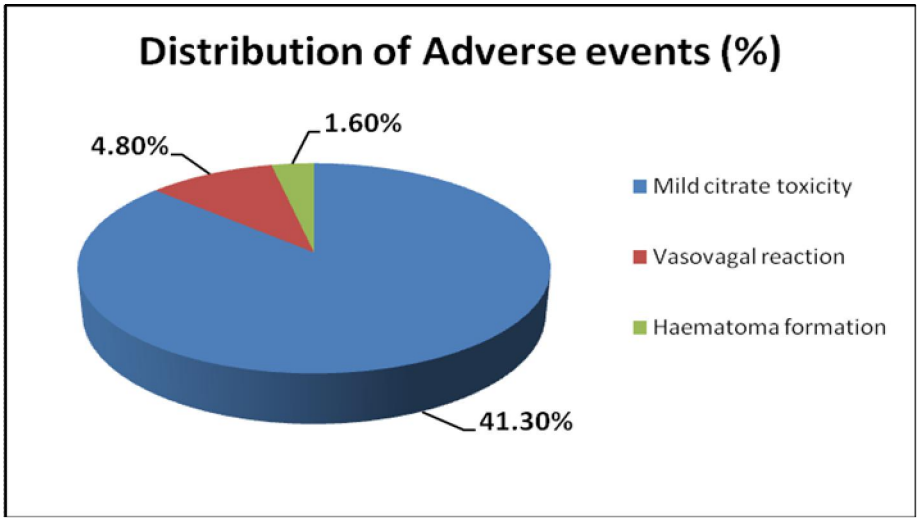

Fig 9: Distribution of Adverse events among plateletpheresis donors (%)

Adverse events vs Previous donations

Out of 63 donors, 32 donors were classified under oral calcium group and the remaining 31 donors classified under intravenous calcium group. A total of 30 adverse events (47.6%) were observed. Out of 30 adverse events, the most common adverse event was mild citrate toxicity (26 out of 30 events) followed by vasovagal reaction (3 out of 30 events) and haematoma formation (1 out of 30 events).The distribution of events among 1st time apheresis donors and repeat apheresis donors are as follows

Table 13: Distribution of Adverse events among 1st time apheresis donors (n=57) & repeat donors (n=6) - Oral Ca^{2+} group and IV Ca^{2+} group

S. No.	Adverse event	Oral Ca^{2+} group (32)		Total (30)	IV Ca^{2+} group (31)		Total (0)
		1st time donors (30)	Repeat Apheresis Donors (2)		1st time donors (27)	Repeat Apheresis Donors (4)	
1.	Mild citrate toxicity	24 (75%)	2 (6.3%)	**26 (81.3%)**	-	-	-
2.	Mild Vasovagal reaction	1 (3.1%)	-	**1** (3.1%)	-	-	-
3.	Moderate Vasovagal reaction	2 (6.3%)	-	**2** (6.3%)	-	-	-
4.	Haematoma formation	1 (3.1%)	-	**1** (3.1%)	-	-	-
Total		**28 (87.5%)**	**2 (6.3%)**	**30 (93.8%)**	-	-	-

IV. Correlation of Donor Adverse events & various parameters

(A) Citrate Toxicity

Table 14: Distribution of mild citrate toxicity symptoms

Route of prophylactic calcium administration	No. of donors MANIFESTED with mild citrate toxicity (26)	No. of donors NOT MANIFESTED with mild citrate toxicity (37)
IV Calcium	0	31
Oral Calcium	26	6

Out of 63 plateletpheresis donors, 26 donors manifested with symptoms of mild citrate toxicity and the remaining 37 donors did not manifest the symptoms. All 26 donors manifesting symptoms of mild citrate toxicity belonged to the Oral Ca^{2+} group. Out of 37 donors not manifesting with symptoms of mild citrate toxicity, 6 donors belonged to the Oral Ca^{2+} group and the remaining 31 donors belonged to the IV Ca^{2+} group.

Correlation of Mild Citrate toxicity with Haematological & Procedural parameters

No citrate related adverse events were observed in the IV Ca^{2+} group (n=31).

Table 15: Correlation of mild citrate toxicity with haematological & procedural parameters in Oral Ca^{2+} group (n=32)

	No. of donors MANIFESTED with mild citrate toxicity (26)	**No. of donors NOT MANIFESTED with mild citrate toxicity (6)**
Pre-proc.PLT count [x 10^3/µL]	263.04±47.93	285.83±80.90
Weight [Kg]	76.73±10.64	84.83±20.87
BMI	25.9± 3.08	28.52±6.33
Return Rate [ml/min]	88.46±12.87	80.00±21.91
Duration [min]	82.23±14.80	62.50±41.62
No. of cycles	6.04±0.96	3.83±2.48
ACD-A reinfused [ml]	284.08±43.71	188.17±87.29
Blood volume processed [ml/min]	2645.85±416.84	1654.83±1005.88
Platelet Yield [x 10^{11}/unit]	3.21±0.20	2.10±1.53

Correlation of Mild Citrate toxicity with Biochemical parameters:

No citrate related adverse events were observed in the IV Ca^{2+} group (n=31).

Table 16: Comparison of Biochemical profile with mild citrate toxicity in Oral Ca^{2+} group (n=32)

	No. of donors MANIFESTED with mild citrate toxicity (26)		**No. of donors NOT MANIFESTED with mild citrate toxicity (6)**	
Parameters	**Pre-proc.**	**Post-proc.***	**Pre-proc.**	**Post-proc.***
S.Ca^{2+} [mg/dL]	10.08±1.04	9.70±0.92	11.40±3.02	10.62±1.04
S.i.Ca^{2+} [mmol/L]	1.18±0.10	1.07±0.10	1.67±0.06	1.20±0.10
S.Mg^{2+} [mg/dL]	2.10±0.23	2.05±0.22	2.23±0.50	2.18±0.31

***** values after intervention with oral calcium supplements

Table 17: Comparison of Biochemical profile with mild citrate toxicity among all plateletpheresis procedures

Parameters	No. of donors MANIFESTED with mild citrate toxicity (26)			No. of donors NOT MANIFESTED with mild citrate toxicity (37)			P-value bet. (a) & (b)
	Pre-proc.	Post-proc.*	Diff. (a)	Pre-proc.	Post-proc.*	Diff. (b)	
S.Ca^{2+} [mg/dL]	10.08±1.04	9.70±0.92	0.38±0.83	10.49±1.71	10.28±0.90	0.21±1.54	0.612
S.i.Ca^{2+} [mmol/L]	1.18±0.10	1.07±0.10	0.11±0.12	1.09±0.23	1.12±0.14	(-) 0.04±0.26	**0.013 (<0.05)**
S.Mg^{2+} [mg/dL]	2.10±0.23	2.05±0.22	0.06±0.26	2.15±0.27	2.15±0.17	0.01±0.28	0.483

***** values after intervention with calcium supplements (both oral and intravenous calcium infusion drip with normal saline)

Table 18: Correlation of calcium tablets in the Oral Ca^{2+} group *(n=32)* **with S.Ionised Calcium levels**

No. of Calcium tablets given to donors (Prophylactic +Therapeutic)	No. of donors	Pre-proc. S.iCa^{2+} [mmol/L]	Post-proc. S.iCa^{2+}* [mmol/L]
1(1 + 0)	6	1.17±0.60	1.20±0.10
2 (1 +1)	7	1.24±0.11	1.11±0.11
3 (1+2)	15	1.15±0.93	1.03±0.08
4 (1+3)	3	1.17±0.09	1.14±0.60
6 (1+5)	1	1.10	1.23

* values after intervention with oral calcium supplements

Table 19: Correlation of IV Ca^{2+} group *(n=31)* **with S.Ionised Calcium levels**

	No. of donors	Pre-proc. S.iCa^{2+} [mmol/L]	Post-proc. S.iCa^{2+}* [mmol/L]
IV Calcium group	**31**	1.07±0.25	1.11±0.14

* values after intervention with intravenous calcium infusion drip with normal saline

(B) Vasovagal reactions

Out of 63 plateletpheresis procedures, only 3 vasovagal reactions were reported.

Table 20: Distribution of Vasovagal Reaction in 1st time & Repeat Apheresis Donors.

	1st time donors (n=57)	**Repeat Apheresis donors (n=6)**	**Total (63)**
Mild Vasovagal reaction	1 (1.6%)	-	1 (1.6%)
Moderate Vasovagal Reaction	2 (3.2%)	-	2 (3.2%)
Severe Vasovagal Reaction	-	-	-
Total	**3**	**-**	**3**

(C) Haematoma formation

Table 21: Distribution of Haematoma formation in 1st time & Repeat Apheresis Donors.

	1st time donors (n=57)	**Repeat Apheresis donors (n=6)**	**Total (63)**
Haematoma formation	1 (1.6%)	-	1 (1.6%)

Discussion

Table 22: Comparison of Haematological & Biochemical parameters across various studies

Parameters /Studies		Present study *(n=61)*	Tenorio *et al*[61] *(n=20)*	Beyan *et al*[49] *(n=265)*	Sachdeva P *et al*[28] *(n=171)*	Chaudhary R *et al*[9] *(n=457)*	Mahmood WHM *et al*[34] *(n= 76)*	Solanki *et al*[10] *(n=60)*	Suresh *et al*[5] *(n=90)*	S.S.Das *et al*[33] *(n=20)*	Mane *et al*[47] *(n=62)*
Hb	**Pre**	**14.81**	-	14.92	15.3	13.5	14.9	-	14.8	-	-
	Post	**14.56***	-	14.00	15.6	12.8	14.7	-	14.5	-	-
Hct	**Pre**	**46.83**	-	43.67	42.7	40.2	44.6	-	43.29	-	-
	Post	**46.33***	-	41.15	43.4	37.7	44.1	-	41.64	-	-
RBC	**Pre**	**5.09**	-	-	-	-	-	-	5.08	-	-
	Post	**5.05***	-	-	-	-	-	-	4.12	-	-
WBC	**Pre**	**7445**	-	7.331	-	7.7	7.1	-	8.28	-	-
	Post	**7428***	-	6.177	-	6.4	7.5	-	6.95	-	-
PLT	**Pre**	**263.81**	238	257	241	231	264.0	-	280.34	-	-
	Post	**203.25***	169	174	170	168	193.4	-	175.58	-	-
MPV	**Pre**	**9.09**	7.6	-	10	8.6	10.0	-	8.61	-	-
	Post	**9.00***	6.8	-	9.8	8.7	9.7	-	8.72	-	-
PDW	**Pre**	**16.05**	-	-	37.3	14.4	12.3	-	15.96	-	-
	Post	**16.10***	-	-	37	14.3	11.8	-	16.27	-	-
S.Ca^{2+}	**Pre**	**10.32**	-	-	-	-	-	9.83	-	2.62	-
	Post	**10.04***	-	-	-	-	-	9.42	-	2.36	-
S.i.Ca^{2+}	**Pre**	**1.12**	-	-	-	-	-	-	-	1.33	-
	Post	**1.10***	-	-	-	-	-	-	-	0.84	-
S.Mg^{2+}	**Pre**	**2.13**	-	-	-	-	-	2.36	-	0.89	2.43
	Post	**2.11***	-	-	-	-	-	2.25	-	0.79	2.16

* values after intervention with calcium supplements (both oral and IV Ca^{2+} infusion with normal saline)

Table 23: Comparison of Procedural Parameters across various studies

Procedural parameters	Present study *(n=63)*	Solanki A *et al*[10] *(n=60)*	Barbosa MH *et al*[56] *(n=316)*	Bueno JL *et al*[23] *(n=51)*	Col Swarup D *et al*[22] *(n=80)*	Das SS *et al*[33] *(n=20)*
Duration [min]	81.29	-	73	74.3	71.47	93.9
Blood volume processed [ml]	2689.59	3490	2829.8	3072	2501.97	2930
Platelet yield [x 10^{11}/unit]	3.22	-	3.47	-	3.33	2.88
Platelet volume [ml]	311.86	-	299.55	-	235.92	-
Return rate [ml/min]	87.94	-	-	-	-	-
Saline used [ml]	233.71	-	-	-	-	-
ACD-A used [ml]	283.92	307.6	360	271	-	275
Total Blood Volume[ml]	5283.17	-	-	-	-	-
No. of cycles	6.05	-	-	-	-	-

Table 24: Comparison of adverse events across various studies

Adverse events/studies	Present study (n=63)	McLeod *et al*[52] (n=428)	Patidar GK *et al*[60] (n=500)	Despotis *et al*[55] (n=19,736)	Crocco *et al*[57] (n= 2,641)	Shakoor HA *et al*[6] (n=200)	Barbosa MH *et al*[56] (n=316)	Philip J *et al*[71] (n=3,120)	Winters JL *et al*[68]	Khajuria K *et al*[72] (n=66)	Rout DR *et al*[73] (n=1,708)
Overall adverse event	**47.6%**	2.18%	18%	0.81%	-	2%	4.4%	2.7%	12%	6.06%	5.86%
Mild citrate toxicity	**41.3%**	-	9%	0.31%	0.38%	-	2.2%	0.17%	0.4%	3.03%	46.1%
Severe citrate toxicity	**-**	1.04%	-	0.04%	-	-	-	-		-	-
Vasovagal reaction	**4.8%**		0.8%	0.39%	0.68%	2.5%	0.6%	0.11%	0.13%	1.51%	12.73%
Haematoma formation	**1.6%**	1.15%	7.4%	0.53%	-	0.5%	1.6%	0.34%	1.15%	1.51%	19.6%
Others	-	-	0.8%	0.22%	-	-	-	1.96%	-	-	-

DISCUSSION

Globally, blood transfusion services have seen a major change in the process of blood donation through the advent of automated technologies. There has been a constant demand for recruitment of donors and a mismatch in the demand-supply chain of blood components as seen in the statistics issued by World Health Organisation.[17, 19] Hence, blood transfusion services need to maintain a fine balance between a good donor base and optimal with rational usage of platelet products, a scarce resource material.

The UK guidelines on blood transfusion services, 2005 state the minimum weight for the apheresis donors to be 50 kg and the same is recommended for apheresis donation by US FDA guidelines. However, the DGHS Standards[2 (p235)] states - '*Donor undergoing an occasional apheresis procedure (performed not frequently than once every 4 week) must meet the same criteria as a whole blood donation*'. Hence, our study may aid in formulating the guidelines for conduction of successful plateletpheresis procedure.[44, 58]

In the present study, donor safety issues were assessed by studying the changes in the haematological, biochemical, procedural parameters and correlating them with occurrence of adverse events.

Demographic profile

A total of 63 donors had undergone plateletpheresis procedure during the study period using Haemonetics MCS+ cell separator. In the present study, mean age of all plateletpheresis donors was observed to be 29.51±7.02 years with majority

of the donors belonging to the younger age group: 21-30 years (n=40; 63.5%) as seen in a similar study conducted by Suresh B *et al*[5] (n=55;61.1%) **[Fig. 4].**

In the present study, the mean weight was 78.73±11.43 Kgs similar to a study conducted by Mangwana S *et al*[59] (77.32±23.53) but was higher than the studies conducted by Sachdeva *et al*[28] (72±11.1) and Patidar *et al*[60] (71.86±9.79) **[Fig.5].**

In the present study, the mean BMI was 26.73±3.39 with majority belonging to Pre-Obese category based on WHO classification, i.e., 25.00 – 29.99 (n=36; 57.14%) similar to a study conducted by Mangwana S *et al*[59] (26.80±8.32). Maximum plateletpheresis procedures performed belonged to Human Blood Group "B" Rh "D" positive (n=32; 50.8%). **[Fig.6 & 7]**

All plateletpheresis donors in our study population were males similar to studies conducted by Suresh B *et al*[5] and Patidar *et al*[60]. Voluntary blood donation among female gender is low in our ethnic population. The major reasons might be attributed to the prevailing anaemic status of our female population failing to meet the minimal eligibility requirements (i.e. Hb<12.5 g/dL), poor venous access and reduced awareness as compared to the male gender[60] **[Table 3].**

Out of 63 donors, most of the apheresis donors were first time donors (n=57; 90.5%) which was similar to a study conducted by Tendulkar A *et al*[13] (n=2037; 94.8%) but was higher as compared to a study done by Patidar *et al*[60] (n=301; 60.2%).This highlights the level of awareness regarding plateletpheresis procedure among voluntary blood donors raising the need for creation of more awareness

regarding the benefits & consequences of plateletpheresis procedure and working towards the need for recruitment of plateletpheresis donors[7] **[Table 4].**

Impact of plateletpheresis donation on various parameters

Out of 63 plateletpheresis donors, 32 donors were given prophylactic oral calcium (Ca^{2+}) supplementation and the remaining 31 donors were given intravenous (IV) calcium (Ca^{2+}) infusion drip with normal saline**.**

In the present study, we observed a statistically significant decline (p value <0.05) in haemoglobin level (14.81±1.24vs14.56±1.29) and platelet count (263.81±54.50 vs 203.25±47.20); but none of the donors experienced any clinical evidence of anaemia or thrombocytopenia. This observation is in concurrence with studies conducted by Suresh *et al.*[5]; Das SS *et al.*[9]; Sachdeva *et al.*[28]; Mahmood WHM *et al.*[34]**;** Beyan *et al.*[49] and Tenorio *et al.*[61] where they had also found a statistically significant decrease in the post procedure haemoglobin and platelet count. **[Table 5 & 22].**

In the present study, one donor had a post procedure platelet count <100 x 10^9/L, but fortunately with no clinical manifestations of thrombocytopenia, similar to studies conducted by Suresh B *et al.*[5] and Das SS *et al.*[9]

In the present study, there were a significant decrease in the post procedure levels of haematocrit (46.83 ± 4.07 vs 46.33 ± 3.83) and WBC count (7445.56 ± 1740.64 vs 7428.25 ± 1737.66). However, in a study conducted by Das SS *et al.*[9] there was a statistically significant decrease in post procedure haematocrit, WBC count as compared to the pre-procedure levels **[Table 5 & 22].**

On comparing the two supplementation groups **[Table 6]**, there was a statistically significant decrease in the mean levels of haemoglobin (14.48 ± 1.14 vs 14.04 ± 1.17) and haematocrit (46.88 ± 3.43 vs 46.33 ± 3.56) in the IV Ca^{2+} supplementation group. Also, in both the groups, there was a statistically significant decrease in platelet count (*Oral Ca^{2+} group:* 267.31 ± 54.68 vs 209.36 ± 54.02; *IV Ca^{2+} group:* 260.19 ± 54.98 vs 196.94 ± 38.84).

In the present study, there was no statistically significant difference ($p>0.05$) in RBC count (5.09 ± 0.50 vs 5.05 ± 0.51), mean platelet volume (9.09 ± 0.90 vs 9 ± 0.90), platelet distribution width (16.05 ± 0.32 vs 16.10 ± 0.43) similar to studies conducted by Das SS *et al.*[9] and Sachdeva P *et al.*[28] **[Table 5 & 22].**

The possible reasons for the decrease in post procedure haemoglobin and haematocrit are as a result of haemodilution due to infusions of citrate solutions and saline; blood loss in the void volume of apheresis kit, technique applied and mechanical haemolysis by the pressure pumps. A significant and sustained decrease in post procedure platelet count is expected following plateletpheresis but without clinical manifestations of anaemia or thrombocytopenia. However, low or borderline pre-donation platelet count (150-200 x 10^3/µL) and haemoglobin (12.5 – 13.0 g/dL) need to be assessed and monitored after the procedure for any decrement in haematological parameters.[5, 9]

In the present study, a significant decrease was observed in S.Calcium (10.32 ± 1.47 vs 10.04 ± 0.95), S.Ionised calcium (1.12 ± 0.19 vs 1.10 ± 0.13) and S.Magnesium (2.13 ± 0.25 vs 2.11 ± 0.20) levels, but was not statistically significant. However, studies conducted by Solanki A *et al.*[10]; Das SS *et al.*[33]; Mane

VB *et al.*[47] reported a statistically significant reduction in post procedure levels of S.Calcium, S.Ionised calcium and S.Magnesium. This variation is attributed to the prophylactic intervention in the form of oral calcium and intravenous calcium infusion drip with normal saline, provided to the plateletpheresis donors **[Table 7 & 22].**

In the present study, on comparing the two supplementation groups **[Table 8]**, we observed a statistical significant decline (1.17 ± 0.09 vs 1.10 ± 0.11) of S.Ionised calcium levels in the oral Ca^{2+} supplementation group with a significant increase (1.07 ± 0.25 vs 1.11 ± 0.14) in the IV Ca^{2+}supplementation group, but within the critical limit of development of hypocalcemic symptoms . Also, there was a significant decline in the mean levels of S.Calcium (*Oral Ca^{2+}group*: 10.33 ± 1.62 vs 9.88 ± 1.00; *I.V Ca^{2+} group*: 10.31 ± 1.33 vs 10.21 ± 0.88) and S.Magnesium (*Oral Ca^{2+}group*: 2.13 ± 0.30 vs 2.07 ± 0.24) with no difference observed in the mean level of S.Magnesium (2.14 ± 0.22 vs 2.14 ± 0.14) in the IV Ca^{2+} group**.**

The possible reasons for the decrease in the post procedure level of serum ionised calcium in the oral Ca^{2+} group and a corresponding increase in the IV Ca^{2+} group might be attributed to the level and mode of calcium supplementation which are dose limited, and a better bioavailability of IV calcium infusion drip with normal saline as compared to the oral calcium supplements.[12, 62]

In the present study, the mean duration of the procedure observed was 81.29 ± 19.24 minutes which was higher than that observed in studies conducted by

Col Swarup D *et al.*[22] (71.47 min); Bueno JL *et al.*[23] (74.3 min); Barbosa MH *et al.*[56] (73 min) and lower in a study conducted by Das SS *et al.*[33] (93.9 min)**[Table 9&23].**

In the present study, the mean blood volume processed was 2689.59 ± 617.4 ml which was lower than that observed in studies conducted by Barbosa MH *et al.*[56] (2829.8 ml); Bueno JL *et al.*[23] (3072 ml); Solanki A *et al.*[10] (3490 ml); Das SS *et al.*[33] (2930 ml) and higher in a study conducted by Col Swarup D *et al.*[22] (2501.97 ml) **[Table 9 & 23].**

In the present study, the mean platelet yield (x 10^{11}/unit) observed was 3.22, similar to a study conducted by Col Swarup D *et al.*[22] (3.33). The values observed was lower as compared to a study conducted by Barbosa MH *et al.*[56] (3.47) and higher in a study conducted by Das SS *et al.*[33] (2.88) **[Table 9 & 23].**

In the present study, the mean product platelet volume observed was 311.86 ml, which was higher as compared to the studies conducted by Barbosa MH *et al.*[56] (299.55 ml) and Col Swarup D *et al.*[22](235.92 ml) **[Table 9 & 23].**

In the present study, the mean ACD – A anticoagulant solution used was observed to be 283.92 ml, similar to studies conducted by Bueno JL *et al.*[23] (271 ml) and Das SS *et al.*[33] (275 ml) but was lower than the values observed in studies conducted by Barbosa MH *et al.*[56] (360 ml) and Solanki A *et al.*[10] (307.6 ml) **[Table 9 & 23].**

On comparing the procedural parameters between the two groups **[Table 10]**, there was a significant higher values observed in procedural parameters (duration of procedure, no. of cycles, return rate, ACD-A reinfused, blood volume

processed, saline used, platelet yield and product platelet volume) in the IV Ca^{2+} group as compared to the oral Ca^{2+} group. Also, there were no citrate related adverse events observed in the IV Ca^{2+} group. This reiterates the fact that although there is an increase in the procedural parameters in the IV Ca^{2+} group, the intervention of slow intravenous calcium infusion drip with normal saline nullifies the effects of citrate related hypocalcemic symptoms due to its better bioavailability leading to improved donor comfort with better production of mean platelet yield and mean product platelet volume [10, 48, 63].

In the present study **[Table 11]**, the pre-procedure platelet count between 1.5 to 2.5 lakhs/ µl had an average of 92 minutes to complete the procedure whereas; the donors with a count between 2.5 to 4.5 lakhs/ µl completed the procedure within the average time of 75 minutes (p value < 0.05).To complete the procedure for the donors with the pre-procedure platelet count between 1.5 to 2.5 lakhs/ µl and 2.5 to 4.5 lakhs/ µl was around 7 and 5 cycles respectively(p value < 0.05).The pre-procedure platelet count between 1.5 to 2.5 lakhs/ µl resulted in a mean platelet yield of 3 x 10^{11}/ unit whereas; the donors with a count between 2.5 to 4.5 lakhs/ µl resulted in a mean platelet yield of 3.3 x 10^{11}/unit (p value < 0.05). Similar observations were also observed in studies conducted by Mangwana S *et al.*[59]; Arun *et al.*[37]**;** Goodnough *et al.*[51]; Das SS *et al.*[64]; Guerrero-Rivera *et al*[65] Enein *et al.*[66] and Chaudhry RC *et al.*[67]**.**

Correlation of Adverse events with various parameters

The overall adverse event observed during plateletpheresis donations was 47.6% (30 out of 63 procedures) which was higher than the studies conducted by

Patidar *et al.*[60] (18%) and Winters JL *et al.*[68] (12%). However, lower incidence of adverse events were observed in other studies such as McLeod *et al.*[52] (2.18%); Despotis *et al.*[55] (0.81%); Shakoor HA *et al.*[6] (2%); Barbosa MH *et al.*[56] (4.4%); Philip J *et al.*[71] (2.7%); Khajuria K *et al.*[72] (6.06%) and Rout DR *et al.*[73] (5.86%) **[Table 12 & 24].**

Citrate Toxicity

In the present study, the most common adverse event observed was mild citrate toxicity (41.30%) in the form of tingling, numbness and perioral paresthesias which was higher as compared to other studies conducted by Patidar *et al.*[60] (9%); Barbosa MH *et al.*[56] (2.2%); Khajuria K *et al.*[72] (3.03%) and lower as compared to a study conducted by Rout DR *et al.*[73] (46.1%) **[Table 12 & 24].** All the adverse reactions were observed in oral Ca^{2+} group. None of the adverse reactions were observed in the IV Ca^{2+} group **[Table 13].** Also, no symptoms of severe citrate toxicity like tetany, seizures were observed in either of the supplementation groups. Despotis *et al.*[55] reported only 0.04% as severe citrate toxicity requiring hospitalisation and McLeod *et al.*[52] reported severe citrate toxicity to be 0.09%.

In the present study, majority of mild citrate related events were reported among the 1st time apheresis donors (42.11%) which was higher as compared to the studies conducted by Patidar *et al.*[60] (24.4%) and McLeod *et al.*[52] (0.87%). This might be attributed to the high number of 1st time donors who are more apprehensive and anxious resulting in higher incidence of reporting adverse events **[Table 13].**

Based on symptoms of mild citrate toxicity, the donors *(n=63)* were classified into two groups – "No. of donors MANIFESTED with mild citrate

toxicity" *(n=26)* and "No. of donors NOT MANIFESTED with mild citrate toxicity" *(n=37)*. All 26 donors manifesting symptoms of mild citrate toxicity belonged to the Oral Ca^{2+} group. Out of 37 donors not manifesting with symptoms, 6 donors belonged to the Oral Ca^{2+} group and the remaining 31 donors belonged to the IV Ca^{2+} group **[Table 14].**

Among the oral Ca^{2+} group, correlating mild citrate toxicity with haematological and procedural parameters **[Table 15]**, it was observed in the group – "No. of donors MANIFESTED with mild citrate toxicity", that, reduced pre-procedure platelet count (263.04 ± 47.93 vs 285.83 ± 80.90) with low body weight (76.73 ± 10.64 vs 84.83 ± 20.87) and low BMI (25.9 ± 3.08 vs 28.52 ± 6.33) increased the duration of the procedure (82.23 ± 14.80 vs 62.50 ± 41.62), number of cycles (6.04 ± 0.96 vs 3.83 ± 2.48) and return rate (88.46 ± 12.87 vs 80.00 ± 21.91) resulting in more amount of ACD-A reinfused (284.08 ± 43.71 vs 188.17 ± 87.29) into the donor and larger amount of blood volume processed with citrate anticoagulant (2645.85 ± 416.84 vs 1654.83 ± 1005.88) resulting in a better platelet yield (3.21 ± 0.20 vs 2.10 ± 1.53) but with larger incidence of mild citrate toxicity (n=26).

The above results correlate with the fact that lower body weight and higher ACD-A reinfusion results in less ECF for dilution and lesser mass of tissue to metabolise the citrate as compared to larger donors leading to higher incidence of mild citrate toxicity.[31] Similarly, Bolan CD *et al.*[48] also observed that donors with higher ACD-A rate and volume infusion during plateletpheresis donation were more prone to hypocalcemic reactions as compared to donors with lower rate and volume infusions.

Similarly, among the oral Ca^{2+} group, on comparing the biochemical parameters **[Table 16]**, the pre-procedure levels of S.Calcium, S.Ionised calcium and S.Magnesium was found to be significantly lower among donors who experienced mild citrate toxicity as compared to those who did not experience symptoms. Also, there was a significant decrease in the post procedure levels of S.Calcium, S.Ionised calcium and S.Magnesium in both the groups. In a study conducted by Patidar *et al.*[60] there was a decline in the divalent cation levels within physiological range among the reactors (with mild citrate toxicity) than the non reactors (without mild citrate toxicity), but was found to be not statistically significant.

Further, analysing the biochemical parameters of all 63 donors with mild citrate toxicity**[Table 17]**, there was a statistically significant difference in serum ionised calcium levels, with post procedure drop being observed in the group - "No. of donors MANIFESTED with mild citrate toxicity (n=26)", whereas a post procedure rise was observed in the group - "No. of donors NOT MANIFESTED with mild citrate toxicity (n=37)" respectively (p value <0.05), but within the critical limit for development of hypocalcemic (0.5 mmol/L) & hypercalcemic symptoms (1.75 mmol/L) respectively.[86]

Correlating the number of calcium tablets with serum ionised calcium levels among the oral Ca^{2+} group **[Table 18]**, 6 of the donors maintained serum ionised calcium level within normal range with pre-procedural prophylactic dose of 1 tablet (0.323 g total Ca^{2+} / 125 mg elemental Ca^{2+}), while the remaining 22 donors developed mild citrate toxicity, which was ameliorated by giving additional oral calcium supplements ranging from 1 to 2 tablets (0.646 g to 0.969 g of total Ca^{2+}).

Among the rest of the four donors, 3 donors were given 3 additional tablets (1.292 g of total Ca^{2+}) and the remaining donor was given 5 additional tablets (1.938 g of total Ca^{2+}).

This finding is similar to a study conducted by Bolan CD *et al*[12], where ingestion of 1g of oral Ca^{2+} resulted in minimal adverse effects while ingestion of 2g of oral Ca^{2+} resulted in significant reduction in the severity of paresthesias and a significant, though modest increase in serum ionised calcium levels. Hence, for our population, we may consider providing atleast thrice the minimal dose of oral Ca^{2+} tablets *(each tablet containing 0.323 g of total Ca^{2+} / 125 mg elemental Ca^{2+})* prophylactically to mitigate the symptoms of mild citrate toxicity and enhance better donor comfort.

Similarly, on correlating the IV Ca^{2+} group (n=31) with serum ionised calcium **[Table 19]**, there was a significant increase in post procedure level (1.07 ± 0.25 vs 1.11 ± 0.14), but with no manifestations of mild citrate toxicity. This is attributed to the slow infusion of intravenous calcium drip along with normal saline providing better bioavailability, improved donor comfort and maintenance of serum ionised calcium levels within the normal range.

This finding is similar to a study conducted by Bolan CD *et al.*[63] on leukapheresis procedures, where prophylactic calcium infusions reduced clinically significant paresthesias by 96%, safely attenuating the marked metabolic effects of citrate administration resulting in a faster and more comfortable procedure. However, cardiac monitoring is required while placing the donors on prophylactic

IV Ca^{2+} infusion drip with normal saline due to the inherent risk of developing cardiac arrhythmias and precipitation of cardiac arrest.[87]

Also, low body weight and BMI observed in our ethnic population are lower as compared to the Western population (Caucasians), similar to a study conducted by Hur Y-M *et al.*[74], implying the fact that additional care in preventing donor adverse reactions and facilitating recruitment of repeat plateletpheresis donations is required during donor selection for plateletpheresis procedures, especially 1st time apheresis donors.

(B) Vasovagal reactions (VVR)

In the present study, the second most common adverse event observed was vasovagal reactions (4.8%) which was higher than studies conducted by Shakoor HA *et al.*[6] (2.5%); Patidar *et al.*[60] (0.8%); Despotis *et al.*[55] (0.39%); Crocco *et al.*[57] (0.68%); Barbosa MH *et al.*[56] (0.6%); Philip J *et al.*[71] (0.11%); Winters *et al.*[68] (0.13%); Tomita *et al.*[75] (0.99%) and Khajuria K *et al.*[72] (1.51%). However, one study by Rout DR *et al.*[73] reported a higher incidence of vasovagal reactions (12.73%) **[Table 12 & 24].**

Out of the overall 30 adverse events noted, all the 3 events (4.8%) observed as vasovagal reactions (2 events – moderate VVR and 1 event – mild VVR) were noted in 1st time apheresis donors which was higher as compared to study conducted by Patidar *et al.*[60] (0.03%) **[Table 20].**

All the vasovagal reactions were observed in the middle of the plateletpheresis procedure. One procedure with mild vasovagal reaction was

completed successfully with concomitant adequate hydration and oral intake of fluids. The other two procedures with moderate vasovagal reactions had to be stopped immediately and could not be continued. Necessary care to the donor was provided by placing the donor in the Trendelenburg position and upon recovery was provided with plenty of oral fluids.

The reason for the occurrence of vasovagal reaction was attributed to the apprehensive/anxious nature of 1st time apheresis donors and the subsequent hypovolemic status during the procedure. Further, occurrence of vasovagal reactions were prevented by making certain modifications in the standard operating procedures: (i) by changing the posture of the apheresis donor from reclining position to the recumbent (supine) position at a lower level than the level of the device, thus avoiding the line of sight reducing the fear of anxiety and thus diminishing the excessive parasympathetic drive; (ii) distracting the donor by playing soft music or using visual media (TV) reducing the parasympathetic drive.[46,76,77]

Haematoma formation

In the present study, out of 30 adverse events , the least common adverse event observed was haematoma formation (1.6%) which was lower than studies conducted by Shakoor HA *et al.*[6] (0.5%); McLeod *et al.*[52] (1.15%); Patidar *et al.*[60] (7.4%); Despotis *et al.*[55] (0.53%); Barbosa MH *et al.*[56] (1.6%); Philip J *et al.*[71] (0.34%); Winters *et al.*[68] (1.15%); Tomita *et al.*[75] (0.99%); Khajuria K *et al.*[72] (1.51%) and Rout DR *et al.*[73] (19.6%) **[Table 12 & 24].** The occurrence of haematoma formation was due to donor related causes, especially seen in 1st time

apheresis donors as compared to repeat donors **[Table 21].** Haematoma formation occurred during the return of the 1st cycle. The procedure was terminated since, the donor experienced concomitant vasovagal reaction. Necessary care was provided to the donor and haematoma treated.

The possible reason might be due to non compliance of instructions issued to the donor leading to inappropriate arm movement resulting in needle displacement and haematoma formation.[60] Haematoma formation is more common in 1st time donors as compared to the repeat donors, since 1st time apheresis donors are more anxious and are not familiar with the harvesting procedure leading to higher incidence of haematoma formation similar to studies conducted by McLeod *et al*[52] and Patidar *et al*.[60] Another reason was due to inaccessibility to median cubital vein leading to poor venous access. The other reasons which could lead to haematoma formation, not found in our study, are phlebotomist error which requires proper competent training of all apheresis personnel.

Summary

SUMMARY

In our study,

- A total of 63 Plateletpheresis donors were divided into two groups – one group of 32 donors were given oral calcium supplements and the other group of 31 donors were given slow intravenous calcium infusion drip with normal saline, and was evaluated for the changes in pre- and post procedural haematological and biochemical parameters. These changes along with procedural parameters were correlated with donor adverse reactions.

- The mean age of the plateletpheresis donors was 30 years and all were males.

- The mean BMI of plateletpheresis donors belonged to "Pre-Obese" category (26.73) based on WHO Classification of Body Mass Index (BMI).

- Out of 63 plateletpheresis donors, 57 donors (90.5%) were 1st time apheresis donors.

- The mean platelet pre-procedural count was 2.63 lakhs/µl and post-procedural count was 2.03 lakhs/µl, which was statistically significant with "P" value of <0.05.

- The mean haemoglobin pre-procedural value was 14.8 g/dL and post-procedural value was 14.6 g/dL, which was also statistically significant with "P" value of <0.05.

- On comparing the oral and intravenous calcium supplementation groups, we observed a significant decrease in serum ionised calcium levels in the oral calcium group from 1.17 mmol/L to 1.10 mmol/L whereas; in the intravenous group we observed an increase from 1.07 mmol/L to 1.11 mmol/L (p value < 0.05).

- The pre-procedure platelet count between 1.5 to 2.5 lakhs/ µl had an average of 92 minutes to complete the procedure. Whereas the donors with a count between 2.5 to 4.5 lakhs/ µl completed the procedure within the average time of 75 minutes (p value < 0.05).

- To complete the procedure for the donors with the pre-procedure platelet count between 1.5 to 2.5 lakhs/ µl and 2.5 to 4.5 lakhs/ µl was around 7 and 5 cycles respectively(p value < 0.05).

- The pre-procedure platelet count between 1.5 to 2.5 lakhs/ µl resulted in a mean platelet yield of 3 x 10^{11}/ unit whereas; the donors with a count between 2.5 to 4.5 lakhs/ µl resulted in a mean platelet yield of 3.3 x 10^{11}/unit (p value < 0.05).

- Among 63 Plateletpheresis donors, 28 donors manifested with adverse reactions. Among 28 donors, one donor had both mild citrate toxicity & vasovagal reaction and another donor had both vasovagal reaction and haematoma formation.

- The most common adverse event observed was hypocalcemic symptoms due to mild citrate toxicity (41.3%) followed by vasovagal reactions (4.8%) and haematoma formation (1.6%).

- Among the prophylactic intravenous calcium supplementation group of 31 donors, none of them experienced any symptoms of citrate toxicity.

- Among the prophylactic oral calcium supplementation group, provided with one tablet each, 26 out of 32 donors developed symptoms of mild citrate toxicity.

- Further in oral calcium supplementation group, 6 of the donors maintained serum ionised calcium level within normal range with pre-procedural prophylactic dose of 1 tablet (0.323 g total Ca2+ / 125 mg elemental Ca^{2+}), while the remaining 22 donors developed mild citrate toxicity, which was ameliorated by giving additional oral calcium supplements ranging from 1 to 2 tablets (0.646 g to 0.969 g of total Ca^{2+}). Among the rest of the four donors, 3 donors were given 3 additional tablets (1.292 g of total Ca^{2+}) and the remaining donor was given 5 additional tablets (1.938 g of total Ca^{2+}).

- Donors who weighed around 76 kg and BMI of 26 manifested with mild citrate toxicity compared to those donors who weighed around 85 kg and BMI of 29.

Conclusion

CONCLUSION

In our study, we observed better bioavailability of serum ionised calcium among Plateletpheresis donors who had been administered prophylactic IV calcium compared to oral calcium supplementation. This fact has further been reiterated by absence of adverse reactions in this group.

However, if oral prophylactic calcium supplementation is preferred, administration of 2 – 3 tablets of calcium (0.969 g of total Ca^{2+} / 375 mg of elemental Ca^{2+}) most often prevents manifestations of mild citrate toxicity.

This enables frequent, smooth and comfortable collection of higher concentration of platelets from a single donor and reduces patient's exposure to multiple donors.

However, it is imperative to conduct more studies with larger number of donors to observe donor adverse reactions specific to our population.

Limitations

LIMITATIONS

- Long term studies on magnesium levels and magnesium supplements following plateletpheresis procedure need to be conducted to assess the safety profile of donors following hypomagnesemia.

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Annexures

THE TAMIL NADU DR. MGR, MEDICAL UNIVERSITY,
CHENNAI-600032
Institutional Ethics Committee

Proposal No: ECMGR0309052 Date: 19.09.2016

CERTIFICATE

This is to certify that the project **No. ECMGR0309052** entitled **"A study on Correlation of adverse reactions with changes in Biochemical, haematological and procedural parameters in plateletpheresis donors."** submitted by **Dr V. Naveen Kumar, DEPARTMENT OF TRANSFUSION MEDICINE** has been approved by the Institutional Ethics Committee, at the meeting held on **15-07-2016,** under the following terms and conditions.

a. This approval is valid for three years or the duration of the project whichever is less from the date of the Certificate.

b. All procedures to be used on participants are professionally acceptable and standardized.

c. All adverse events during the course of study must be recorded and reported to the IEC within a period of seven days

d. Any change in the study procedure/site/investigator should be informed to the IEC.

e. A yearly progress report of the project has to be submitted to the IEC for review.

(Dr. S. Mini Jacob)
Member Secretary
Institutional Ethics Committee
The Tamil Nadu Dr MGR Medical University

CANCER INSTITUTE (W.I.A)

(REGIONAL CANCER CENTRE)
INSTITUTIONAL ETHICS COMMITTEE
Reg. No. ECR/235/Inst/TN/2013
Adyar, Chennai - 600 020.
Phone : 044-22209150 Extn : 129, Fax : 044-22354508
E-mail : iec@cancerinstitutewia.org

Ethics Committee Re-Registration No.ECR/235/Inst/TN/2013/RR-16 Date :

Reference Number: IEC/2017/05

31 May 2017

To,
Dr. V. Naveen Kumar
IInd Year,
Post Graduate Student in M.D (IH &BT)
Dept. of Transfusion Medicine
The Tamil Nadu Dr. M.G.R Medical University
Guindy, Chennai -32

Subject: Ethics Committee Approval Letter

Reference: A study on correlation of adverse reactions with changes in biochemical, haematological and procedural parameters in platelet pheresis donors.

Dear Dr. Naveen Kumar,

This is with reference to your letter dated 30 January 2017 for review of the above referenced project proposal. The ethics committee reviewed the following documents,

1) Post Graduate Dissertation Protocol
2) Ethics Committee Approval letter from the Tamil Nadu Dr.M.G.R. Medical University Dated 19.09.2016
3) Approval Copy of Scientific Advisory Committee, Cancer Institute(W.I.A) dated 02.01.2017
4) Proforma
5) Donor Information Sheet (English)
6) Donor Information Sheet (Tamil)
7) Informed Consent Form (English)
8) Informed Consent Form (Tamil)
9) Executive Summary of Project Proposal

The following members of the ethics committee were present at the ethics committee meeting held on 04 March 2017 at 2.30 pm at Board Room, IORT building, Dr. Krishna Murthy Campus, Cancer Institute(W.I.A), Chennai.

S.No	Name	Designation/ Role of member in the ethics committee	Affiliation of the member with Institution	Attendance to the meeting
1	Dr. V.I. Mathan	Chairman	Not affiliated with cancer Institute	Present
2	Dr. T.G. Sagar	Member Secretary	Affiliated with Cancer Institute	Present
3	Dr.G. Selvaluxmy	Clinician	Affiliated with Cancer Institute	Present
4	Dr. V. Sridevi	Clinician	Affiliated with Cancer Institute	Present
5	Dr.V.K. Ramadesikan	Basic Medical Scientist	Not affiliated with Cancer Institute	Absent
6	Dr. Niranjali Devaraj	Scientific Member	Not affiliated with Cancer Institute	Absent
7	Dr. K. Kalaichelvi	Clinician	Not affiliated with Cancer Institute	Present
8	Mr. M. Suresh	Legal Expert	Not affiliated with Cancer Institute	Present
9	Mrs. Ranganayaki Kumar	Lay Person	Not affiliated with Cancer Institute	Present
10	Dr. S. Padma	Legal Expert	Not affiliated with Cancer Institute	Absent
11	Mr. Chaganti V. K. Maitreya	Social Scientist	Not affiliated with Cancer Institute	Present

The above documents were reviewed and the study was approved by the ethics committee, to be conducted in its presented form.

CANCER INSTITUTE (W.I.A)

(REGIONAL CANCER CENTRE)
INSTITUTIONAL ETHICS COMMITTEE
Reg. No. ECR/235/Inst/TN/2013
Adyar, Chennai - 600 020.
Phone : 044-22209150 Extn : 129, Fax : 044-22354508
E-mail : iec@cancerinstitutewia.org

Date :

The ethics committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information sheet/ informed consent and asks to be provided a copy of the final report.

Yours Sincerely,

Dr. T.G. Sagar
Member Secretary
Institutional Ethics Committee

Institutional Ethics Committee
Chennai
600 020
Cancer Institute (WIA)

URKUND

Urkund Analysis Result

Analysed Document: A STUDY ON CORRELATION OF ADVERSE REACTIONS WITH CHANGES IN BIOCHEMICAL, HAEMATOLOGICAL AND PROCEDURAL PARAMETERS IN PLATELETPHERESIS DONORS.docx (D31205238)
Submitted: 10/11/2017 7:50:00 AM
Submitted By: naveen.varadan@gmail.com
Significance: 1 %

Sources included in the report:

EVALUATION OF BLOOD UTILIZATION PRACTICES IN NEONATES.doc (D31142861)
http://docplayer.net/18768517-Definitions-abc-page-1-of-8-bonfils-blood-center-dr-078-prd-rev-5-donor-reaction-injury-intervention-protocol.html

Instances where selected sources appear:

4

CERTIFICATE – II

This is to certify that this dissertation work titled **"A STUDY ON CORRELATION OF ADVERSE REACTIONS WITH CHANGES IN BIOCHEMICAL, HAEMATOLOGICAL AND PROCEDURAL PARAMETERS IN PLATELETPHERESIS DONORS"** of the candidate **Dr. V. NAVEEN KUMAR** with registration number **201531002** for the award of **M.D.** in the branch of **IMMUNOHAEMATLOGY AND BLOOD TRANSFUSION**. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **1** percentage of plagiarism in the dissertation.

Guide & Supervisor sign with SEAL.

The Tamil Nadu Dr. M.G.R. Medical University

Department of Transfusion Medicine

Licence No. 191/28C

BLOOD DONOR FORM

APHERESIS DONOR QUESTIONNAIRE

THE TAMIL NADU Dr. M.G.R. MEDICAL UNIVERSITY

Blood Bag No.	Date	Group & Rh

PERSONAL PARTICULARS

Donor's Name	Age : D.O.B. :	Sex : Male / Female

Residential Address	Office Address
.....	.....
.....	.....
.....	.....
.....Mobile/Ph :	.....Mobile/Ph : .....
Email :	Email : .....

KIND ATTENTION

Kindly furnish the following information sought on medical grounds as per Government Notification. If any question is felt embarrassing kindly bear with us

TEMPORARY DEFERRAL, IN THE PAST 12 MONTHS HAVE YOU

- ☞ Received Tranfusion of Blood or its products Y/N
- ☞ Suffered from Hepatitis or had Hepatitis Immunoglobulin or had close contact with an individual suffering from Hepatitis Y/N
- ☞ Had exposure to tattoos, acupunture or body piercing? Y/N
- ☞ Had antirabies vaccine or was treated for dog bite? Y/N
- ☞ Undergone any major surgery or met with any major accident? Y/N

IN THE PAST 6 MONTHS HAVE YOU EVER

- ☞ Suffered from Typhoid / Cholera / Acute infection of kidney or Bladder Y/N
- ☞ Had delivery / had pregnancy / any abortion / or been breast feeding? Y/N / N/A*
- ☞ Had any minor surgery or met with any minor accident? Y/N

* N/A - Not applicable

IN THE PAST 3 MONTHS

- ☞ Have you donated blood, plasma or platelets? Y/N
- ☞ Have yow been treated for malaria? Y/N

IN THE PAST 2 MONTHS

- ☞ Have you had any history of measles, mumps and chickenpox? Y/N

IN THE PAST 1 MONTH

- ☞ Had treatment for acne with Isotretinoin? Y/N
- ☞ Had Anti tetanus serum, Anti venom serum, Anti diphtheria serum, Anti gas gangrene serum or Rubella vaccination? Y/N

IN THE PAST 3 WEEKS

- ☞ Have you had tooth extraction or any dental procedure? Y/N

IN THE PAST 2 WEEKS

- ☞ Have you had chicken pox, shingles, measles, mumps or yellow fever vaccination Y/N

IN THE PAST 1 WEEK

- ☞ Have you had cortisone for treatment? Y/N
- ☞ Had history of diarrhea with fever? Y/N

IN THE PAST 4 DAYS

- ☞ Have you had IV antibiotics? Y/N

IN THE PAST 3 DAYS

- ☞ Have you had oral antibiotics? Y/N

IN THE PAST 24 HOURS

- ☞ Have you had alcoholic drinks Y/N
- ☞ Are you an aircrew, a heavy machine vehicle driver, a construction worker? Y/N
- ☞ Are you reporting for duty in the next 12 hours? Y/N
- ☞ Are you suffering from cold, cough, sore throat or acute sinusitis? Y/N

PERMANENT DEFERRAL

H/o. Uncontrolled blood pressure or stroke?	Y/N
H/o. Heart disease or arrhythmias?	Y/N
H/o. Epilepsy or anticonvulsants?	Y/N
H/o. Auto immune disease or immounsuppressive therapy?	Y/N
H/o. Abnormal bleeding tendencies?	Y/N
H/o. Diabetes mellitus on treatment with insulin or hypoglycemic drugs?	Y/N
H/o. Chronic liver disease or endocrine disorders?	Y/N
H/o. Parkinsons diseases?	Y/N
H/o. Psorasis or treatment for the same?	Y/N
H/o. Psychiatric disorders?	Y/N
H/o. Major surgeries for kidney, heart, liver or brain?	Y/N
H/o. Severe allergic disorders or asthmatic on steroid therapy?	Y/N
H/o. IV drug abuse, heterosexual/homosexual promiscuity / STD?	Y/N

GENERAL QUESTIONS

1. Have you donated blood? Y/N
2. When was your last blood donation? .....

   How many times have you donated? .....
3. Are you willing to donate for emergency situations? Y/N
4. Have you had any reactions like giddiness/fainting attacks/ fits after donation? Y/N
5. Any history of unexplained weight loss/ chronic cough / fever / diarrhoea / Lymph nodes enlargement? Y/N

DECLARATION

I hereby declare that the above information is true to the best of my knowledge and this consent of mine to be a blood donor is voluntary. I understood that certain tests (HIV, HCV, HBV, SYPHILIS, MALARIA), will be performed on my blood for the purpose of ensuring the safety.

I would like to know the results, if any positive. Y/N

I am aware that I am donating platelets by apheresis technique and the procedure and side effects of Plateletpheresis as explained to me. I hereby give my consent / willingness to under go this procedure.

Date : Signature of donor

Wt. (in Kg)	HB gm %	PR	BP	RR	TEMP.	CVS	RS	CNS	ABD	Skin disease at phlebotomy site

The above donor is FIT / UNFIT to donate blood.

Blood Bag : SINGLE / DOUBLE / TRIPLE / QUADRUPLE

Volume : 350 ml /450 ml

Bag Segment No.	
Sign. of the Phlebotomist	

Remarks :

Signature of the MEDICAL OFFICER.

Haemonetics MCS+ Platelet Collection Procedure Sheet

Donor Name: _____ Donation NO: _____

Date of Birth: _____ I/C No: _____

Blood Pressure: _____ Bar Code: _____

Pulse: _____ Blood Group: _____

Disposable No: _____ Machine: MCS+ Serial No: _____

Lot No: _____ Protocol: Leukodepleted Platelet (LDP)

A/C Type: ACD-A AC Ratio: 1 : 9

Batch No: _____ Expiry Date: _____

HAEMOCACULATOR

	Ht cm	Wtg Kg	Blood Vol	Hct %	Plt Pre-count ($x 10^3$)	Target Plasma Vol	Target Plt Yield	Process Vol	Target Duration

PROCEDURE SHEET

Cycle	Time	Draw/Return ml/min	Plasma Vol	Platelet Vol	Process Vol	NaCl ml/cycle	Remarks
1							
2							
3							
4							
5							
6							
7							
8							

PROCEDURE STATISTIC

Process Vol	Procedure Time (min)	Saline Used ml	Plasma Vol ml	AC used ml	Platelet Vol ml	AC in Plt ml	Est. Plt Yield ($x 10^{11}$)	Target Plt Yeild ($x 10^{11}$)

Platelet Numeration : _____ x 10^3/ul x Platelet Vol = _____ x 10^{11} (Actual Plt Yield)

WBC Numeration : _____ x 10^3/ul x WBC Vol = _____ x10^6(Actual WBC Residual)

Comments: _____

_____

Operator : _____ Signature: _____

தமிழ்நாடு டாக்டர் எம்.ஜி.ஆர் மருத்துவப் பல்கலைக்கழகம்

குருதியேற்றுத் துறை

தமிழ்நாடு டாக்டர் எம்.ஜி.ஆர் மருத்துவப் பல்கலைக்கழகம்

உரிமம் எண் 191/28C

எபெரசிஸ் இரத்ததானப்படிவம்

இரத்தப்பை எண்	தேதி	இரத்தக்கொடையாளர் எண்	இரத்தப் பிரிவு

தனிப்பட்ட விவரங்கள்

இரத்தக் கொடையாளர் பெயர்	வயது : பிறந்த தேதி :	பாலினம் : ஆண் / பெண்

வீட்டு விலாசம் :	அலுவலக விலாசம் :
.....	.....
.....	.....
.....	.....
..... போன் :	..... போன் : .....
இ–மெயில் :	இ–மெயில் : .....

தங்கள் கவனத்திற்கு

அரசு விதிகளின்படி மருத்துவரீதியாக கேட்கப்பட்டுள்ள கீழ்க்கண்ட வினாக்களுக்கு விடையளிக்கவும். ஏதேனும் வினாக்கள் தங்களை மனரீதியாக புண்படுத்தியிருந்தால் தயவுகூர்ந்து பொறுத்துக்கொள்ளவும்.

கடந்த பன்னிரெண்டு மாத காலத்திற்குள்

1. இரத்தம் மற்றும் இரத்தக்கூறுகள் தங்களுக்கு ஏற்றப்பட்டுள்ளதா? ஆம் – இல்லை
2. மஞ்சள் காமாலை நோயினால் பாதிக்கப்பட்டுள்ளீர்களா? இம்மியுனோகுளோபின் தடுப்பூசி போட்டுக் கொண்டுள்ளீர்களா? (அ) மஞ்சள் காமாலை நோயினால் பாதிக்கப்பட்டிருந்த எவரிடமாவது நெருங்கிய தொடர்பு வைத்திருந்தீர்களா? ஆம் – இல்லை
3. உடம்பில் (காது மற்றும் ஏதேனும் உடற்பகுதியில்) பச்சை குத்தி உள்ளீர்களா? ஆம் – இல்லை
4. நாய்க்கடிக்கான தடுப்பூசி போட்டுள்ளீர்களா? (அ) நாய்க்கடிக்காக ஏதேனும் சிகிச்சை எடுத்துள்ளீர்களா? ஆம் – இல்லை
5. பெரிய அறுவை சிகிச்சை ஏதேனும் செய்து கொண்டுள்ளீர்களா? (அ) பெரிய விபத்து ஏதேனும் சந்திக்க நேரிட்டதா? ஆம் – இல்லை

கடந்த ஆறு மாதகாலத்திற்குள்

1. டைப்பாய்டு, காலரா, சிறுநீரக மற்றும் சிறுநீர்ப்பை (கிருமி) நோய்களால் பாதிக்கப்பட்டுள்ளீர்களா? ஆம் – இல்லை
2. சிறிய அறுவை சிகிச்சை ஏதேனும் செய்துகொண்டுள்ளீர்களா? (அ) சிறிய விபத்து ஏதேனும் சந்திக்க நேரிட்டதா? ஆம் – இல்லை

3. மகப்பேறு நடந்துள்ளதா? தாய்மை அடைந்துள்ளீர்களா? கருச்சிதைவு ஏற்பட்டுள்ளதா? தாய்ப்பால் கொடுத்துக் கொண்டிருக்கிறீர்களா? ஆம் – இல்லை

கடந்த மூன்று மாதகாலத்திற்குள்

1. இரத்தம் மற்றும் இரத்தக் கூறுகள் தானம் செய்துள்ளீர்களா? ஆம் – இல்லை
2. மலேரியா நோய்க்கு சிகிச்சை எடுத்துள்ளீர்களா? ஆம் – இல்லை

கடந்த இரண்டு மாத காலத்திற்குள்

1. தட்டம்மை, பொன்னுக்கு வீங்கி, அம்மை போன்ற ஏதாவது நோய்களால் பாதிக்கப்பட்டுள்ளீர்களா? ஆம் – இல்லை

கடந்த ஒரு மாத காலத்திற்குள்

1. முகப்பருக்காக ஐஸோடிரட்டினாயின் போன்றஏதேனும் மருந்தை உபயோகப்படுத்தி உள்ளீர்களா? ஆம் – இல்லை
2. நோய் எதிர்ப்பு சக்தி ஊசி (அ) தடுப்பு ஊசி (டெட்டனஸ், பாம்புக்கடி, டிப்தீரியா, கேஸ்கேங்கரின், ரூபெல்லா) ஏதேனும் போட்டுள்ளீர்களா? ஆம் – இல்லை

கடந்த மூன்று வார காலத்திற்குள்

1. பல் சிகிச்சை ஏதேனும் செய்து கொண்டுள்ளீர்களா? ஆம் – இல்லை

கடந்த இரண்டு வார காலத்திற்குள்

1. அம்மை / அக்கி / தட்டம்மை / பொன்னுக்கி வீங்கி / (எல்லோ) காய்ச்சல் போன்ற நோய்களுக்கு தங்களுக்கு தடுப்பூசி ஏதேனும் போடப்பட்டுள்ளதா? ஆம் – இல்லை

கடந்த ஒரு வார காலத்திற்குள்

1. காய்ச்சலுடன் கூடிய வயிற்றுப்போக்கு ஏற்பட்டுள்ளதா? ஆம் – இல்லை
2. (ஸ்டீராய்டு) கார்ட்டிஸோன் மாத்திரை எடுத்துள்ளீர்களா? ஆம் – இல்லை

கடந்த நான்கு நாட்களுக்குள்

1. நரம்பு வழியாக ஏதேனும் ஆண்ட்டிபயாட்டிக் மருந்து எடுத்துள்ளீர்களா? ஆம் – இல்லை

கடந்த மூன்று நாட்களுக்குள்

1. வாய் வழியாக ஏதேனும் ஆண்ட்டிபாயடிக் மருந்து எடுத்துள்ளீர்களா? ஆம் – இல்லை

கடந்த 24 மணி நேரத்திற்குள்

1. மது அருந்தி உள்ளீர்களா? ஆம் – இல்லை
2. தாங்கள் வான்ஊர்தி (அ) கனரக வாகனங்களின் ஓட்டுநர்களா? ஆம் – இல்லை
3. கட்டுமானப் பணி செய்பவர்களா? ஆம் – இல்லை
4. அடுத்த 12 மணி நேரத்திற்குள் தாங்கள் தங்கள் பணியில் ஈடுபட வேண்டியுள்ளதா? ஆம் – இல்லை
5. காய்ச்சல், சளி, இருமல், தொண்டைப்புண், சைனஸ் போன்றவைகளினால் அவதியுறுகிறீர்களா? ஆம் – இல்லை

பொதுவான சில வினாக்கள்

1. இரத்த தானம் செய்துள்ளீர்களா?
   அவ்வாறெனில் எப்பொழுது..... எத்தனை முறை..... ஆம் – இல்லை

2. தாங்கள் உணவு அருந்திய நேரம் .....

3. அவசரக் காலங்களில் இரத்த தானம் செய்ய விருப்பம் கொண்டுள்ளீர்களா? ஆம் – இல்லை

4. இரத்த தானத்தின் போது மயக்கம் அடைந்துள்ளீர்களா? வலிப்பு ஏற்பட்டுள்ளதா?
(அ) உடல் சம்பந்தமான உபாதைகள் ஏதேனும் ஏற்பட்டதா? ஆம் – இல்லை

5. காரணம் இல்லாமல் எடை குறைவு, தொடர் இருமல், காய்ச்சல், பேதி, உடற்பகுதியில் ஏதேனும் வீக்கம் (அ) ஊசியினால் காயம் போன்றவைகள் ஏற்பட்டுள்ளதா? ஆம் – இல்லை

நிரந்தரமாக நிராகரித்தல்

1. கட்டுப்படுத்த இயலாத இரத்த அழுத்தம் (அ) பக்கவாதம் போன்றநோய்களில் பாதிக்கப்பட்டுள்ளீர்களா? ஆம் – இல்லை

2. இருதயநோயினால் பாதிக்கப்பட்டுள்ளீர்களா? ஆம் – இல்லை

3. வலிப்பு நோயினால் பாதிக்கப்பட்டுள்ளீர்களா? அவ்வாறெனில் அதற்கான சிகிச்சை எடுத்துக்கொண்டிருக்கிறீர்களா? ஆம் – இல்லை

4. எதிர்ப்புத்திறன் சம்பந்தமான நோய்களால் பாதிக்கப்பட்டுள்ளீர்களா? எதிர்ப்புத்திறன் குறைக்கும் மருந்துகள் ஏதேனும் எடுத்துக்கொண்டிருக்கிறீர்களா? ஆம் – இல்லை

5. இயல்புக்கு மாறான இரத்தக்கசிவு ஏதேனும் ஏற்பட்டுள்ளதா? ஆம் – இல்லை

6. சர்க்கரை நோய்க்காக இன்சுலின் ஊசி (அ) அதற்காக மாத்திரை ஏதேனும் எடுத்துக்கெண்டிருக்கிறீர்களா? ஆம் – இல்லை

7. கல்லீரல் நோய் உள்ளதா? நாளமில்லாச் சுரப்பி குறைப்பாடு ஏதேனும் உள்ளதா? ஆம் – இல்லை

8. பார்க்கின்சன்ஸ் (நடுக்கம்) நோயினால் பாதிக்கப்பட்டுள்ளீர்களா? ஆம் – இல்லை

9. சோரியாஸிஸ் (தோல்) நோயினால் பாதிக்கப்பட்டு சிகிச்சை எடுத்துக்கொண்டிருக்கிறீர்களா? ஆம் – இல்லை

10. மனநலம் பாதிக்கப்பட்டுள்ளதா? ஆம் – இல்லை

11. சிறுநீரகம், இருதயம், கல்லீரல் மற்றும் மூளை போன்றபகுதிகளில் பெரிய அறுவை சிகிச்சை ஏதேனும் செய்து கொண்டுள்ளீர்களா? ஆம் – இல்லை

12. ஒவ்வாமை, ஆஸ்துமா போன்றநோய்களுக்கு ஸ்டீராய்டு சிகிச்சை எடுத்துக்கொண்டிருக்கிறீர்களா? ஆம் – இல்லை

13. நரம்பு வழி போதை மருந்து பழக்கம், தகாத உடலுறவுப் பழக்கம், பால்வினை நோய்கள் போன்றவைகள் ஏதேனும் உள்ளதா? ஆம் – இல்லை

உறுதிமொழி

என்னால் அளிக்கப்பட்டுள்ள அனைத்து தகவல்களும் உண்மை எனவும், எனது விருப்பத்தின் பெயரில் எபெரசிஸ் லம் தட்டணுக்கள் வழங்குவதற்கு சம்மதம் என்று உறுதியளிக்கின்றேன். எபெரசிஸ் செயல்முறையும் அதனால் ஏற்படும் பக்கவிளைவுகளையும் மருத்துவர் லம் அறிந்தேன். பாதுகாப்பு கருதி எனது இரத்தமானது (எச்.ஐ.வி., எச்.சி.வி., எச்.பி.வி., சியிலிஸ், மலேரியா) போன்ற நோய்களால் பாதிக்கப்பட்டுள்ளதா என்பதைக் கண்டறிய பரிசோதனைகளுக்கு உட்படுத்தப்படும் என்பதை அறிவேன்.

மேற்கூறிய பரிசோதனைகளின் முடிவுகளைத் தெரிந்துகொள்ள விரும்புகிறேன். ஆம்-இல்லை

தேதி: கொடையாளர் கையொப்பம்

Wt. (in Kg)	HB gm %	PR	BP	RR	TEMP.	CVS	RS	CNS	ABD	Skin disease at phlebotomy site

The above donor is FIT / UNFIT to donate blood.

Blood Bag : SINGLE / DOUBLE / TRIPLE / QUADRUPLE

Volume : 350 ml /450 ml

Bag Segment No.	
Sign. of the Phlebotomist	

Remarks :

Signature of the MEDICAL OFFICER.

DONOR INFORMATION SHEET

A STUDY ON CORRELATION OF ADVERSE REACTIONS WITH CHANGES IN BIOCHEMICAL, HAEMATOLOGICAL AND PROCEDURAL PARAMETERS IN PLATELETPHERESIS DONORS

Apheresis is a procedure where whole blood removed from the body is passed through an apparatus that separates out one (or more) particular blood constituent and returns the remainder of the constituents back into the individual's circulation. This study is done to analyse the variations in biochemical, haematological and procedural parameters and to correlate these parameters with donor adverse reactions.

PROCEDURE:

Two (2) samples, each of 5 ml blood will be taken from a vein (other than the one chosen for the Plateletpheresis procedure) before the start of the procedure and at the end of the procedure. The blood samples will be tested for various biochemical and haematological parameters and will be recorded in the Proforma sheets.

BENEFITS AND RISKS:

There are minimal risks involved for the donors in the form of tingling sensation around the mouth, vasovagal reactions and hematoma formation during the procedure which are treated by calcium supplementation, fluid management and by selecting a clean vein respectively.

Very rarely, the donor may experience severe forms of hypocalcemia in the form of tetanic seizures which are treated by intravenous calcium supplementation. In case of occurrence of severe adverse effects, the procedure will be stopped immediately.

CONFIDENTIALITY:

Your privacy will be protected as permitted by the law. Only your researcher and Ethical Committee members will have access to the data collected during the study.

PARTICIPATION:

Your participation in this study is purely voluntary and you are free to decide now or later whether to continue or discontinue from the study.

NAME OF THE DONOR:

SIGNATURE :

DATE :

இரத்தக் கொடையாளருக்கான தகவல் படிவம்

பிளேட்லெட்பெரசிஸ் கொடையாளரின் உயிர் வேதியியல், குருதியியல் மற்றும் செய்முறை அளவுருக்களில் உண்டாகும் மாற்றங்களுக்கும் கொடையாளரின் எதிர்மறை நடவடிக்கைகளுக்கும் உண்டான தொடர்பு - ஒரு ஆய்வு.

ஒருவரது உடலில் இருந்து "முழுமையான இரத்தம்" பிரித்து எடுக்கப்பட்ட பின் அதை ஒரு கருவியின் உள்ளே செலுத்தி, குறிப்பிட்ட ஒன்று அல்லது மேற்பட்ட இரத்தத்தின் மூலக்கூறுகளை தனிமைப்படுத்தி, மீதமுள்ள பிற மூலக்கூறுகளை மறுபடியும் உடல் இரத்த ஓட்டத்தில் கலக்கச் செய்வதற்கான செயல்முறை "அபேரிசிஸ்" என்று அழைக்கப்படுகிறது.

இந்த ஆய்வின் நோக்கம் யாதெனில் பிளேட்லெட்பெரசிஸ் கொடையாளரின் உயிர் வேதியியல், குருதியியல் மற்றும் செய்முறை அளவுருக்களில் ஏற்படும் மாறுபாட்டிற்கும், அன்னாருக்கு ஏற்படும் எதிர்மறை நடவடிக்கைகளுக்கும் உண்டான தொடர்பை ஆய்வு செய்வதுமாகும்.

செய்முறை:

மேற்சொன்ன செயல்முறைக்கு முன்பும், பின்பும் இரத்த கொடையாளரின் இரத்த நாளத்தில் இருந்து (பிளேட்லெட்பெரசிஸ் செய்முறைக்காக நிர்ணயம் செய்யப்பட்ட இரத்தக் குழாய் தவிர) 5 மிலி அளவில் இருமுறை இரத்தம் பரிசோதனைக்காக எடுக்கப்படும். இந்த இரதத்தில் பல்வேறு உயரி வேதியியல் மற்றும் குருதியியல் அளவுருக்கள் ஆய்வு செய்யப்பட்டு, செய்முறை அளவுருக்களோடு படிவங்களில் பதிவு செய்யப்படும்.

எதிர்மறை விளைவுகள்:

இரத்தக்கொடையாளருக்கு ஏற்படும் எதிர்மறை விளைவுகள் மிகக்குறைவே. அவையாதெனில் வாயை சுற்றி ஏற்படும் கூச்ச உணர்ச்சி மற்றும் தலைச்சுற்றல், இரத்தக்கட்டு. மேற்சொன்னவை, கால்சியம் மாத்திரை கொடுத்தல், திரவ மேலாண்மை மற்றும் தெளிவான இரத்த நாளத்தை தேர்வு செய்தல் மூலம் சரிசெய்யப்படும். ஏதேனும் கடுமையான எதிர்மறை விளைவுகள் உண்டாகுமேயானால், இச்செய்முறை உடனடியாக நிறுத்தப்படும்.

இரகசியக் காப்பு:

சட்டத்தில் அனுமதிக்கப்பட்டவாறு உங்களுடைய தனியுரிமை பாதுகாக்கப்படும். இந்த ஆய்வின் மூலம் சேகரிக்கப்படும் அனைத்து விவரங்களும் உங்களது ஆராய்ச்சியாளர் மற்றும் நெறிமுறைக்குழு உறுப்பினர்களுக்கு மட்டுமே தெரியவரும்.

பங்கேற்பு:

இந்த செய்முறை ஆய்வில் உங்களது பங்கேற்பு முற்றிலும் உங்களுடைய விருப்பத்தைச் சார்ந்தது. இந்த ஆய்வில் தொடர்ந்து பங்கேற்பது அல்லது விலகிச் செல்வது பற்றி, இப்பொழுதோ அல்லது பின்னரோ முடிவு எடுக்க தங்களுக்கு உரிமை உண்டு.

கொடையாளரின் பெயர் :

கையொப்பம் :

தேதி:

CONSENT

I confirm that I have read and understood the information about the above research study (Donor Information Sheet) dated _____ and I received chance to ask the questions.

My participation in this study is purely voluntary and I know that I am free to withdraw from the study at any time, without giving any reason and without affecting my legal rights.

I understand that the procedure will take approximately 45-90 minutes. To prevent clotting during the procedure, citrate anticoagulant will be added to the blood being processed.

I agree that small samples of my blood will be drawn for laboratory parameters and testing done to reduce the risks of infectious disease transmission.

I have been informed that the risks are similar to those involved in a whole blood donation such as vasovagal reactions, hematoma formation. In addition to these risks, I understand the possible adverse effect resulting from the citrate effect/toxicity includes tingling sensations in the fingers or lips, numbness, tremors, muscle cramping, feelings of anxiety, or all of the above. In case of occurrence of severe adverse effects, the procedure will be stopped immediately.

I agree to this access. I know that my identification will not be revealed in any of the details that is released to the third persons or published.

I agree not to restrict or interfere with any data or results that are obtained from this study.

I agree to participate in this research study for the above listed purpose.

Donor's Name :
Signature : Date:

Signature of the person
Who obtains the consent : Date:
Donor ID No :

ஒப்புதல் படிவம்

மேற்சொன்ன ..... நாளது செய்முறை ஆய்வு குறித்த தகவல்களை (இரத்தக் கொடையாளருக்கான தகவல் படிவம்) நான் படித்து அறிந்து புரிந்து கொண்டேன் என இதன் மூலம் உறுதியளிக்கிறேன். இது குறித்து கேள்விகள் கேட்பதற்கும் எனக்கு வாய்ப்பு அளிக்கப்பட்டதையும் உறுதி செய்கிறேன்.

இந்த ஆய்வில் என் பங்கேற்பு முற்றிலும் என் விருப்பம் சார்ந்தது என்பதை அறிந்து கொண்டேன். எந்தக் காரணமும் குறிப்பிடாமல் எனது சட்ட உரிமை பாதிக்கப்படாத வண்ணம் இந்த ஆய்விலிருந்து, எப்பொழுது வேண்டுமானாலும் விலகிக்கொள்ள எனக்குரிமை உண்டு என்பதையும் அறிந்து கொண்டேன்.

இந்த செய்முறை 45-90 நிமிடங்கள் வரை எடுக்கும் என்பதை அறிந்து கொண்டேன். இந்த செய்முறையின் போது கருவியில் செலுத்தப்பட்டுள்ள இரத்தம் உறையாமல் இருப்பதற்காக சிட்ரேட் (anti coagulant) சேர்க்கப்படுகிறது என்பதை அறிந்து கொண்டேன்.

இந்த ஆய்வின் போது, என்னுடைய இரத்தத்தை (சிறிதளவில்) ஆய்வக அளவுருக்கள் மற்றும் கிருமிகள் பரிசோதனைக்கு தர நான் ஒப்புக்கொள்கிறேன்.

முழு இரத்தக் கொடையளிப்பின் போது ஏற்படும் தலைசுற்றல் இரத்தக்கட்டு போன்ற எதிர்மறை விளைவுகள், இச்செய்முறையின் போதும் உண்டாக வாய்ப்புள்ளது என்பதை அறிந்துகொண்டேன். சிட்ரேட் நச்சுத்தன்மையினால், வாயை சுற்றி கூச்ச உணர்வு, மறத்தல்,

தசைபிடிப்பு, நடுக்கம், பதற்றம் போன்ற எதிர்மறை விளைவுகள் உண்டாக வாய்ப்புள்ளது என்பதை அறிந்து கொண்டேன். ஏதேனும் கடுமையான எதிர்மறை விளைவுகள் உண்டாகுமேயானால், இச்செய்முறை உடனடியாக நிறுத்தப்படும் என்பதை அறிந்துகொண்டேன்.

இந்த செயல்முறை ஆய்வுக்கு நான் ஒத்துழைப்பு நல்குகிறேன் என்று வாக்களிக்கிறேன். இந்த ஆய்வுத்தகவல்கள், மூன்றாவது நபர்களுக்கோ அல்லது விளம்பரத்திற்காக வெளியிடப்படும் போதோ, எனது அடையாளம் (அ) தனித்துவம் தெரிவிக்கப்படமாட்டாது என்பதையும் நான் அறிந்து கொண்டேன்.

இந்த ஆய்வின் மூலம் பெறப்படும் யாதொரு தகவல் அல்லது முடிவுகளைத் தடை செய்யவோ அல்லது குறுக்கிடவோ மாட்டேன் என்று உறுதியளிக்கிறேன். மேற்கூறிய குறிக்கோளை அடைய எடுத்துக்கொள்ளும் இந்த செய்முறை ஆய்வில் பங்கேற்க நான் முழுமனதுடன் சுயநினைவுடன் சம்மதிக்கிறேன்.

கொடையாளரின் பெயர் :

கையொப்பம் : தேதி:

ஒப்புதல் பெறுபவரின் கையொப்பம்: தேதி:

கொடையாளரின் அடையாள எண் :

PROFORMA

I. Demographic Profile:

Name of the donor: Age/Sex: **Donor ID No:**

Height: cm Weight: Kg BMI: kg/m^2

Blood Group: Bag No.:

II. Donor History & Physical Examination:

(a) Total no. Of donations done till date (*excluding the present donation*):

	Whole Blood donation	**Apheresis donation**
Total no. Of donations		
Last Donated on		

(b) Whether satisfying Donor Selection criteria as per Drug & Cosmetics Act, 1940 and Rules,1945 – Yes/No

(c) Physical Examination:

BP: mm Hg PR: /min RR: /min Temp:

CVS: RS: CNS: Abd: Skin:

(d) Screening Test:

HIV – 1&2: Reactive/Non-reactive
Hep – B : Reactive/Non-reactive
HCV : Reactive/Non-reactive
RPR : Reactive/Non-reactive
Malaria : Positive/Negative

III. Quantitative Analysis:

(a) Analysis of Biochemical & Haematological parameters:

Time of collection of 2nd sample:_____ min from end of procedure

S.No.	Haematological/Bio-chemical parameter	Pre-plateletpheresis procedure	Post-plateletpheresis procedure
1.	Hb (g/dl)		
2.	Hct (%)		
3.	RBC Count (million cells/cu.mm)		
4.	WBC Count (cells/cu.mm)		
5.	Platelet Count($x10^3/\mu L$)		
6.	MPV (fL)		
7.	PDW (%)		
8.	S.Ca^{2+} (mg/dl)		
9.	S.i Ca^{2+} (mg/dl)		
10.	S.Mg^{2+} (mg/dl)		

Hb – Hemoglobin; Hct – Hematocrit;MPV - Mean Platelet Volume; PDW – Platelet Distribution width;S.Ca^{2+}-S.Calcium;S.iCa^{2+}-S.ionised Calcium;S.Mg^{2+} - S.Magnesium

(b) **Analysis of Donor Adverse Reactions:**

Total no. Of chewable Calcium tablets given to the donor:

S.No.	Type of Adverse reactions	CITRATE TOXICITY		Vasovagal reactions	Hematoma formation	Others
		Mild*	Severe**			
1.	Status (Yes/No)					
2.	Intervention provided					
3.	Remarks (If Any)					

**Mild Citrate Toxicity – Circumoral paresthesia*

***Severe Citrate Toxicity – Tetany, hypocalcemic seizures.*

(c)**Analysis of procedural parameters:**

Total Blood Volume = ml

S.No.	Procedural parameter	Pre-plateletpheresis procedure *(Estimated)*	Post-plateletpheresis procedure *(Actual)*
1.	Total no.of cycles (Estimated vs Actual)		
2.	Total duration (min) (Estimated vs Actual)		
3.	Vol. of Saline used (ml)		
4.	Vol. of AC used (ml)		
5.	Volume processed (ml)		
6.	Plasma Volume (ml)		
7.	Platelet yield		

Platelet volume (ml) = AC in Plt (ml) =

Target Plt yield = Est.Plt yield =